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CANCER
CLINICALLY CONSIDERED

J. BLAND-SUTTON, F.R.C.S.



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CANCER CLINICALLY CONSIDERED

BY

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PREFACE

DEGREE-CONFERRING, as well as licensing, bodies require from men and women seeking the legal right to practise surgery, evidence that they have attended a certain number of lectures on systematic surgery. This custom is a survival of the time when text-books were few and rarely good. When it became my duty to deliver lectures for "signing-up purposes," as it is termed by the non-respecting student, I selected each year a subject which deeply interested me, and in regard to which I ventured to hope information could be given supplementing the meagre descriptions accorded to it in current manuals. During the session 1908-9 at the Middlesex Hospital I considered that extraordinary perversion of epithelium which we call cancer. This is a subject of great importance and wide interest; it also possesses an enormous literature. If, as bacteriologists are now teaching, the epithelial covering of the body, within and without, is protective and constitutes the first line of defence against infection, anything which concerns its vulnerability has a personal interest for everybody.

The object of these lectures is to set forth some of the disasters to which men and women are liable when the defensive cells are cancerous and become in consequence a foe of mankind.

JOHN BLAND-SUTTON.

47, BROOK STREET, W.;
October, 1909.

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CANCER CLINICALLY CONSIDERED.

THE CLASSIFICATION AND GENERAL FEATURES OF CANCER.

I.

CANCER belongs to a group of tumours which possess extraordinary interest for surgeons, physicians, and pathologists, because it matters not in what part of the body they arise, these tumours will, if left to themselves, inevitably destroy life. On this account they are termed "malignant."

As nothing is known concerning the cause of malignant tumours it is customary to classify them according to the tissue in which they arise. The body is made up of two great groups of tissues, one known as connective-tissue and the other as epithelium. In addition we make a separate group of the two important tissues of the body—striped or voluntary muscle-fibre, and nerve-tissue. The connective tissues include all such things as fibrous tissue; it does not matter whether it is stout stuff like the periosteum of bone; or the delicate tissue which forms the sustentacular framework of the retina, which is so fine that it requires special preparation to show it, even under the

microscope. Bone, cartilage (gristle), and fat belong to this group. Malignant tumours which arise from the connective tissues are known as "sarcomata."

The epithelial group is also very complex. Epithelium serves two purposes. In certain parts it is protective, for example, where it covers the surface of the skin and the interior of the mouth and lips. In these situations it is of a characteristic shape, and it is usually spoken of as squamous epithelium, but where epithelium permeates organs to form the essential secreting structures as in the case of the mammary glands, the sweat-glands, the liver or kidneys, and other complex organs, including the cells which cover the whole of the alimentary canal from the lips to the anus, it is more or less columnar in shape. Any of this epithelium may take on from some cause, we know not what, malignant action, and form a tumour known as a cancer, which will spread and destroy the life of the person in whom it arises. Thus cancer (or carcinoma) is defined by the pathologist as *a malignant tumour arising in epithelium*. When cancer arises in squamous-celled epithelium it is termed "squamous-celled carcinoma," and occasionally by surgeons as "epithelioma." The latter term is unfortunate, because all cancers are epitheliomata in the sense that they arise in epithelium. German and French writers use the term "epithelioma" in the same general sense in which British surgeons employ the name "carcinoma," so that in order to avoid confusion it will be wise to avoid using the term "epithelioma," and refer to cancer arising in stratified epithelium as squamous-celled carcinoma.

The peculiar flattened cells known as endothelium which line the interior of blood- and lymph-vessels, and cover the surface of serous membranes, such as the pleura, peritoneum, and pericardium, formed a subject of dispute among histologists as to whether they

belonged to the connective tissue or the epithelial group. It is now known that endothelium in any situation may be the source of a malignant tumour, which is known as an endothelioma.

It has also been discovered that the cells which cover the delicate chorionic villi, so conspicuous on the coverings of the early embryo, sometimes undergo malignant change and produce a tumour possessing remarkable and destructive characters, known as *chorion-epithelioma*.

There is a tumour, fortunately rare, which arises in the ovary, known as a malignant teratoma. The ovary contains in each follicle a cell known as the sex-cell or ovum, and when the environment is favourable and this cell is fertilised it may grow up and become a man or a woman. Under certain conditions these sex-cells form the starting-point of a malignant teratoma, and such tumours are almost confined to female infants and girls.

For clinical convenience we are able to divide malignant tumours into five groups: (1) The typical cancers; (2) endotheliomata; (3) chorion-epithelioma; (4) malignant teratoma: these all arise from epithelium and are carcinomata; and (5) sarcomata, which arise in connective tissue.

We begin with the consideration of the common kind of cancers, namely, those which arise in the epithelium of the adult body. These are of two kinds, according to whether the perversion attacks the squamous cells or, those which belong to secreting glands. Cancer arises in any part of the body where there is epithelium. There are certain predisposing conditions: for example, it is liable to arise on the tongue in chronic syphilitic ulcers; at the margin of the lower lip in small fissures and ulcerated surfaces, especially in men and women who smoke dirty clay pipes; at the margin of chronic ulcers and lupus patches; and X-ray burns. On the

conjunctiva it occasionally attacks the scars of old lime burns, and it is very apt to attack an old solitary pigmented wart in any part of the body. In less conspicuous regions of the body it arises in similar chronically diseased parts such as the fissures at the margin of the *os uteri* left after child-birth, in chronic ulcers of the stomach, and in prostate glands which are the seat of chronic disease.

The insidious nature of cancer is perhaps best studied in the female breast, for a woman may have a large cancerous lump in her breast and feel neither pain nor inconvenience, but she will notice that one breast looks a little different from the other—perhaps the nipple is drawn in, or the skin may be dimpled over a part of it, and there is a slight alteration in the contour of the breast. Then she feels and finds there is a small hard lump in it. When such a breast is removed from the body and this lump, which constitutes the primary cancerous focus, is divided, you will find it impossible to accurately define its limits, for it passes indefinitely into the soft tissues of the breast. This indefiniteness is a most important thing with regard to cancer, because nearly all innocent tumours are enclosed in a soft sac or capsule, which isolates them from the surrounding tissues. In the case of encapsulated tumours you can make an incision into the capsule and turn out the tumour as easily as a ripe banana is removed from its rind. This is not the case with cancers; you cannot, with your naked eye or with your fingers, or with any of the methods which we use in the ordinary way of surgery, not even with the aid of a microscope, define its boundaries. This peculiar lack of limitation of the growth is one of the most characteristic, as well as a dangerous feature of cancer. When you prepare a thin section from the lump in the breast, stain and examine it under the microscope, you will be able to recognise two tissues—the paren-

chyma and the stroma. The latter is made up of fibrous tissue, and the section is divided by it into alveoli, and each alveolus, or hollow, is filled with epithelium. The peculiar point about the epithelium of the cancerous growth is this; that in whatever gland the cancer arises, the epithelium which is found in these alveoli is characteristic of that gland. Thus in the breast the epithelium will have the characteristics of the ordinary cells of the mammary gland: in the uterus the cells will be columnar, exactly like those which line the interior of this organ: when cancer grows in the liver it will have the same kind of structure as the liver-cells, and if it grows in the bile-ducts it will possess epithelium of the same character as that which lines these canals. Indeed, so characteristic are the cells of cancer that when a carefully prepared section is put before a competent morbid histologist he can tell you the part of the body in which the particular cancer arose. Knowledge of this kind is often of great utility in clinical investigation. There was a man in the ward who had some trouble with his abdomen; nobody could quite be certain which organ was affected nor the nature of the disease. In a little while the whole of his skin became dotted with small knots, and then we knew that he was suffering from dissemination of cancer. As it was important to know the primary source, one of these little nodules was excised from the skin, and when examined under the microscope it showed all the characters of the peculiar glands found at the pylorus. We therefore knew at once that in all probability he had a cancer in this region of his stomach. This opinion was verified when the man died a few weeks later. It is only one example of many; you will have plenty of opportunities of seeing all these things demonstrated in practice.

We have now to consider the stroma, which is found

in all cancers except chorion-epithelioma. The nature of this tissue has been particularly investigated. The stroma which forms around these cells is probably a protective effort of the connective tissue excited by the activity of malignant epithelium. It is now the fashion to speak of this as the connective-tissue reaction. You know you may get a shot in your body, or a piece of needle in your finger, or some such thing. When the foreign body is clean the tissues will tolerate it, but they throw round that foreign body a capsule of connective tissue. You can study this process in the peritoneal cavity. It sometimes happens that we often swallow with our food foreign bodies, such as a minute piece of mill-stone, perhaps a small fragment of a pot, or even the point of a needle or of a pin. If the small foreign body makes its way through the bowel into the general peritoneal cavity and it is not septic, it will cause a good deal of irritation, and some fluid and cells known as lymph will be thrown out around the body, and it will become embedded in stuff like so much gum. In the course of time this exuded material will organise into fibrous tissue; by degrees it will become encysted and form the nucleus of a round ball of organised fibrous tissue, and thus rendered innocuous. The same thing takes place around the advancing columns of cancer, for their invasion of the adjacent parts leads to an active formation of connective tissue which invests them. This production of new tissue around the growing margin of a cancer has led Handley to describe the cancer cell as *an obligate parasite upon the connective tissue cell*. As a rule, primary cancers do not grow to any great size; rarely in the breast do they reach a size larger than an orange, often not larger than a chestnut, for they are poorly supplied with blood-vessels, and the connective tissue contracts upon the epithelial element. Sometimes the tissue contracts so firmly on the columns that the epithelial

cells undergo changes and become absolutely destroyed, and the cancer undergoes spontaneous cure, especially in the breast and in the large intestine. It is this growth of connective tissue which makes the tumour so hard. Although this primary focus undergoes spontaneous cure, it will nevertheless destroy the patient's life in another way. All the malignant tumours are peculiar in that their cells become disseminated. After a primary focus has existed for a few months the cells will implicate the lymphatics which are contained in the connective tissue, and make their way to the nearest lymph-glands. When learning anatomy in the dissecting-room you rarely perceive the importance of the lymphatics and lymph-glands; as a rule, students neglect them in the routine dissecting-room work. In the case of cancer in the breast, the cancer-cells find their way into the mediastinal lymph-glands, the axillary glands, and then creep up and infect those in the neck; they find their way into the thoracic duct, and then enter the blood-stream. The lungs, as you know, are permeated by small blood-vessels, the pulmonary capillaries, where these small cancer-cells are strained from the blood, and implant themselves on to the tissues of the lungs and form what are known as secondary cancers, nodules, or knots. The number of these secondary knots which may be found about the body is extraordinary—two or three hundred or more of them. This process is sometimes termed “metastasis.”

We believed until recently that these secondary knots were entirely due to the dispersal through the body of cancer-cells by the blood-stream. This is known as the embolic theory. Mr. Handley investigated this subject, and has discovered that when cancer forms in the breast, cells creep into the adjacent lymphatics and find their way into the lymphatics in the fascia which covers the thorax, and after invading

the pleura, parietal and pulmonary, spread to the lung. They also make their way towards the epigastrium, and implicate the fascia of the abdomen, extend to the fascia of the limbs and the periosteum of the bones. The cancer spreads from a central spot in widening circles until it has spread over the trunk and the trunk-ends of the limbs, and, if the patient lives long enough, it may even reach the hands and feet. This remarkable process, the truth of which Mr. Handley has practically established, is called "permeation." It is quite certain that, although this theory of permeation explains the greater number of cases of metastases, nevertheless it is true that cancer is also disseminated by means of the blood-vessels, but in a minor degree. Some interesting work has been carried out by Schmidt, of Vienna, on the fate of cancer-cells in the blood. If cancer-cells are distributed through the blood-vessels, surely if we examine the blood of a cancerous patient when dissemination is going on we ought to find them. I have spent a good deal of time and much hard work in trying to find these cells actually in the blood; I have never succeeded; but Schmidt examined the small pulmonary vessels and found cancer particles in them (Fig. 1). His investigation revealed to us the remarkable behaviour of the blood to cancerous particles, for on entering the blood-stream they excite thrombosis, and the thrombus contracting on the emigrant cells may ultimately destroy them. This defending or prophylactic power of the blood is very important, as it prevents the blood-stream from being colonised.

Cancer-cells sometimes find their way into the circulation by directly implicating the thoracic duct. Primary cancer of the stomach infects the lymphatics about the receptaculum chyli, and occasionally converts the thoracic duct into a solid cord, and spreads to the lymph-glands lying in the left posterior triangle of the neck. This is a matter of clinical interest, because some of

you know well that when examining a patient with suspected carcinoma of the abdomen, or a tumour of the stomach, the physician or the surgeon, as the case may be, feels at the root of the patient's neck in order to ascertain if there be an enlarged gland in that situation. Many years ago we were puzzled to know why a man with carcinoma of the stomach should get an enlarged gland in the root of his neck; although we could not explain why it enlarged, we knew it to be a very good diagnostic sign. But here is an explana-



FIG. 1.—A pulmonary capillary in section, showing cancerous emboli in its lumen. (After Schmidt.)

tion of it. The glands in the abdomen become infected with cancer and it spreads along the lymph-vessels to the thoracic duct and thence upwards to the glands in the root of the neck. The thoracic duct has been found converted into a solid cancerous cord secondary to cancer of the rectum.

There is another point concerning which you must disabuse your minds. Most of you believe that cancer is, as a rule, quickly fatal. As a matter of fact, cancer itself is often a slow and very chronic disease, and may take years to kill a patient; in this respect it resembles

leprosy. I spent a Christmas day in the Leper Hospital at Jerusalem, and there was a man in that institution who had had leprosy for thirty years; and I have seen patients in this hospital who have had cancer twenty years, and you will hear of many cases of cancer which have persisted for a long time. It is rarely the primary focus of cancer which kills the patient; it is the secondary growths; they block up the lung and get into the brain and obstruct the blood-vessels. Or, if they are in situations where the air has access to them, micro-organisms will flourish on the dead cancerous tissues, causing them to decompose and slough. These changes lead to septic conditions, such as pneumonia, bronchitis, peritonitis, pyelitis, or some similar terminal infection, which destroys the life of the patient.

CANCER OF THE BREAST.

II.

CANCER of the female breast is a common disease. Indeed, the breast, with the possible exception of the stomach and the uterus, may be regarded as the commonest situation in the body in which cancer occurs. Surgeons have been looking at tumours of the breast since the time of Hippocrates, and even before that, yet at present there is absolutely no unequivocal sign by which we can tell that a patient has cancer of the breast. When the disease is well developed there is, as a rule, no difficulty, but in the early and curative stages you will find that the cleverest, wisest, and most experienced men who look at the breast will often be in considerable doubt as to whether the lump which they feel in it, is really cancer or not. One of the most extraordinary facts which will strike you when you examine these patients is this: that in some cases a cancerous knot in the breast is sometimes scarcely larger than a cherry, while in another case it will form a tumour as big as an orange. Before coal-tar colours were discovered, those who studied pathological histology had great difficulty in differentiating tumours. Now we cut fine sections of tumours and stain them with hæmatoxylin or some coal-tar preparation, such as an aniline dye. This method enables us to classify tumours according to their minute structure. In the days before these methods were known a tumour in the breast was called a "scirrhus"

or "stone cancer" if it were small and hard; when it was large and soft an "encephaloid" or "brain-like cancer," or "medullary cancer"; and if it contained much jelly-like material, a "colloid cancer." But now, by means of the microscope, aided by differential staining, we are able to show that these tumours, although many of them, when they are cut across, do not look like cancer, are found to be so when sectioned and stained. An investigation into the characters of these tumours informs the surgeon whether he is dealing with an innocent or a malignant tumour; and if he is dealing with a malignant tumour it enables him to make what, in ordinary clinical language, we call a prognosis.

The breast varies in size in different individuals. Fat women have enormous breasts, and, as a rule, thin breasts are found in thin women. Sometimes slim women will be found to have large breasts, but a big breast in a thin woman usually consists of a large amount of glandular tissue and a small proportion of fat. The essential element of the breast is the teat, nipple or mamilla. In some persons it is below the surface, and is said to be inverted; in others it is small and prominent, and in those who have borne many children, and suckled them, it is large, thick and fleshy. When you examine the nipple with a magnifying glass you will be able to see the terminal orifices of small ducts; these run from the nipple into the glandular substance of the breast. The large mass of the breast, which rests on the pectoralis major and serratus magnus muscles, is usually spoken of as the body of the breast; it contains the epithelial elements which manufacture the milk. The breast is a compound racemose gland, consisting of about twenty lobules, each of which has its own duct, which traverses the nipple and opens at its tip independently. The ducts terminate in the substance of the breast in what are known as acini. In breasts which have never been

functional the epithelium lining it is so closely apposed as to resemble a solid column; in functional breasts the acini possess comparatively large lumina, and the epithelium is tall and columnar; it is this epithelium which secretes the milk. At the base of the nipple each lactiferous duct presents a dilatation, or ampulla, known as the sinus.

The point I want you to understand is this: A system of epithelium-lined canals terminating in acini, also clothed with epithelium, permeates the breast from the tip of the nipple to the utmost confines of the gland, and from any part of these epithelial canals a malignant tumour may arise. When it develops in the acini of the gland it is spoken of as acinous carcinoma, and is the common kind, but when it develops in the sinuses and ducts near their terminations it is called duct carcinoma, which is an uncommon kind; but it is worth study because it is not so malignant as the acinous form of cancer, and its presence is announced by a very characteristic sign, for the patient complains of a free discharge of blood-stained fluid from the nipple, which is sometimes so abundant that it soaks the clothes. Women often seek relief entirely on account of this blood-stained discharge, and not so much on account of the tumour which they find in their breast, or to any annoyance it may cause them.

Although duct cancer is not so malignant as the acinous form, nevertheless it sometimes recurs. When this happens the recurrences take the cystic form; they appear like over-ripe grapes. Sometimes these little cystic bodies are filled with blood-stained fluid, and possess what is called an intra-cystic process; this process often resembles a small unripe (red) blackberry. So the cystic character of this duct carcinoma is preserved in the recurrences.

I have said that acinous carcinoma may arise in any part of the breast, but the common place in the breast

in which it arises is underneath the nipple. As soon as a patch of acinous carcinoma grows at the base of the nipple the connective-tissue reaction is established, and the fibrous tissue formed in consequence contracts

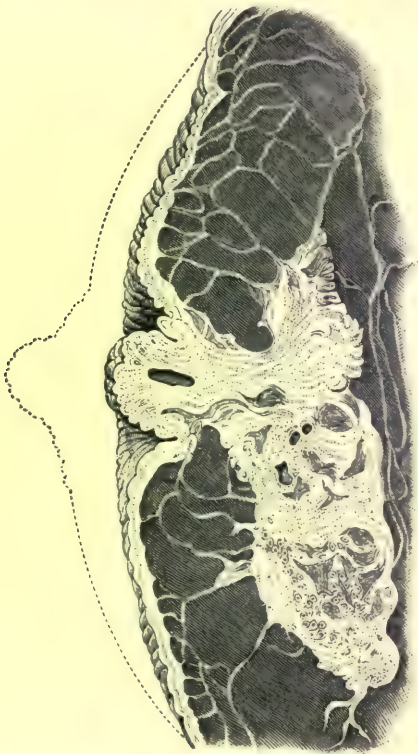


FIG. 2.—A cancerous breast in section showing retraction of the nipple.

as it grows and draws in the nipple. In nine cases out of ten when you look at a cancerous breast, if the carcinoma is in this classical spot, the nipple is found to be retracted, the breast shrunken, and smaller than its fellow. The appearance thus presented resembles the crown of a ripe pippin. Surgeons in examining a

breast always look carefully at the nipple to see whether it is retracted or not. It is necessary to draw attention to this matter, because you must determine whether the nipple is retracted, as in Fig. 2, or inverted, as in Fig. 3. An inverted nipple may be drawn out, but

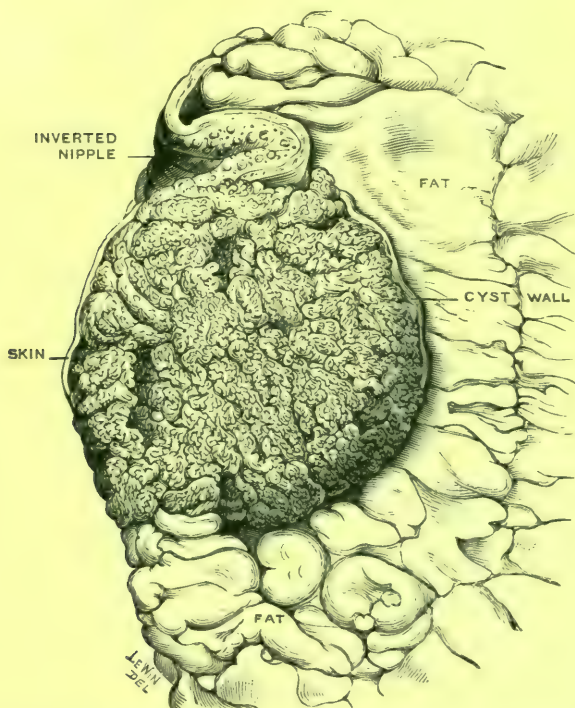


FIG. 3.—A breast with its nipple in section from a case of duct cancer. The nipple is inverted.

the proceeding is painful to the patient, but it is easily and painlessly performed after the breast has been removed, for with a pair of forceps you can draw such a nipple out: this cannot be done with a nipple which is retracted in the ordinary way by carcinoma. An inverted nipple is met with in many individuals, unassociated with disease of the breast, and in others it

is inverted when they suffer from duct carcinoma, or from a cyst in the breast. It is an important thing from the clinical standpoint when you are looking at a breast suspected to contain cancer, and you cannot see the nipple standing out prominently, to make sure whether it is retracted or simply inverted. The specimen represented in Fig. 4 is unusual in regard to this matter. When the patient from whom I removed it was admitted to the hospital, we noticed at once the extreme prominence of the nipple, although that tumour had been growing in the breast, according to her account, for two years. This made us a little suspicious as to whether it really was cancer. As a matter of fact it is not ordinary cancer, but an endothelioma—quite a rare kind. There is another point with regard to the breast to which I must draw your attention, as it concerns the origin of cancer. I have already told you, not only may cancer begin in a lactiferous duct, or in its sinus, or in the acini where they are near the nipple, but they will grow in any part of the breast, even in its most outlying parts; this becomes a matter of some importance, because when you find a lump under the skin near the clavicle, or near its axillary border, or close to the sternum, you may be doubtful whether you are dealing with a tumour of the breast. The bulk of the breast is immediately under the nipple, but on careful examination you will find that it does not form a definite circular mass flat on the chest wall, as you might think from looking at Luschka's drawing which is figured in the text-books on physiology and many text-books of anatomy. The breast possesses three tail-like processes of glandular tissue. One extends towards the sternum—the sternal process; another reaches towards the clavicle—the clavicular process; and a third creeps into the axilla—the axillary process. The matter is further complicated by the presence of some glands in the skin of the axilla, which occasionally enlarge in

lying-in women and secrete milk. Cancer may start in any of the tail-like prolongations of the mammary gland, or in the skin-glands in the axilla (axillary lumps as they are sometimes called).



FIG. 4.—A breast in section; it contains an endothelioma (perithelioma). The nipple is unaffected.

When cancer starts in the periphery of the mammary gland, and especially in an outlying process, it is apt to cause diagnostic doubt, as the following case will show:

A woman was placed under my care by a lady doctor on account of a small lump beneath the skin quite close

to the clavicle. I was uncertain whether the lump which we felt under the clavicle was really carcinoma or not; it was sufficiently suspicious for me to recommend the patient to submit to removal of the breast. She was fifty years of age, and therefore not likely to have any more children, so I strongly advised the patient to be on the safe side and have the breast removed. Women are very unhappy when they are thus advised; the breasts are such an adornment when they are at dinner in evening dress, especially if they possess what is termed an "effective bust." When I see them sitting round a table, each one eyeing her neighbour, I often think of the lines:

"The rich and poor alike their nakedness display;

The poor, because they must, the rich, because they may."

However, if it comes to a question of their health and future life the question has to be settled. This woman took my advice and agreed to part with her breast, and when she lay on the table under the influence of chloroform, and I could feel it distinctly, I had no doubt that it was carcinoma. So I removed the whole breast very thoroughly with the pectoral fascia and the axillary fat and the slightly enlarged axillary lymph-glands. The cancer formed a lump as big as a cherry-stone on the tip of the sternal process of the breast. It may puzzle you to believe why a thing so small as that should wreck the patient's life. It was microscopically examined and found to be typical carcinoma. Another woman had a small knot in an out-of-the-way part of the breast; we examined her in the ward, and felt no doubt in our minds that this patient had a small carcinoma in the breast, but there was no retraction of the nipple. We thought we could feel some axillary glands, and when we came to operate upon them what we thought to be cancer turned out to be a cyst in the breast. As the whole

breast was in the condition known as chronic mastitis, in which the bulk of the breast is replaced by fibrous tissue, and with very little glandular material in it, we had no hesitation in taking away the breast, because it has been shown over and over again that cancer is much more liable to attack diseased organs than those which are healthy. Abnormal conditions of tissues and organs which predispose them to cancer are spoken of as pre-cancerous conditions. Although we are absolutely helpless in curing well-marked cases of cancer, even by operation, we are striving more and more to recognise what are the preceding, or pre-cancerous conditions, so that we can deal with them surgically, before they become cancerous.

Cancer may begin on the tip of the nipple, and I have had under my care a woman whose nipple was completely destroyed by cancer. This is her story: She was in Northumberland Ward three years ago for rheumatism, and I was asked to see her breast because she had some ulceration of the nipple, and I advised her to wait until the physicians cured her rheumatism. If at that time the ulceration continued she had better come and see me again. Ulceration of the nipple usually heals, but in some patients it becomes chronic, and Sir James Paget, who was the greatest authority in his day on cancer and tumours of the breast, pointed out that he had seen a number of these cases of chronic eczema of the nipple become cancerous. He advocated and practised amputation of the breast when patients came under observation with inveterate eczema of the nipple. This particular woman took me literally at my word; the doctors had not managed to cure her rheumatism, and she did not come to me again until the ulceration had completely destroyed the nipple, and its place was occupied by an ulcer surrounded by a ring of hard cancerous tissue. You will naturally say to me: "How is it that, although

it has been growing for three years, there is so little cancerous material?" It is because this cancer has been exposed to the air and has become infected and ulcerated, and as fast as the cancer forms it slowly disintegrates and comes away with the discharge.

I must say a few words about the endothelioma of the breast, which I have already mentioned. The patient was sixty-five and had a movable smooth lump as big as an orange in the breast associated with enlarged

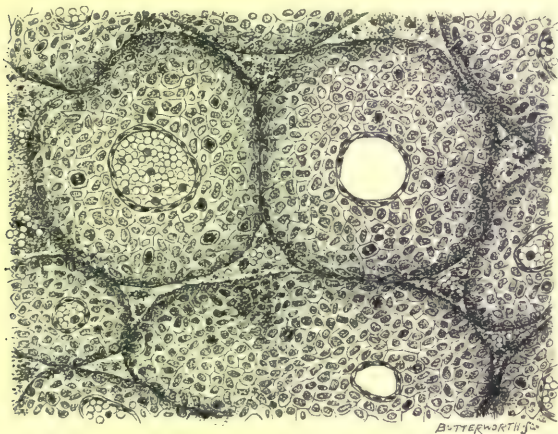


FIG. 5.—The microscopic characters of a perithelioma, showing the cell-mantle around the blood-vessels (after Ziegler).

lymph-glands. We were certain there were no signs of dissemination after examining the liver and lungs and other organs. She had a small trace of albumen in the urine, but we gave her the advantage of an operation. This tumour is really a perithelioma (Fig. 4), a sub-variety of the endotheliomata. These tumours grow from the endothelium lining the inner walls of the blood-vessels in the breast; microscopically they consist of cylinders of malignant cells formed in and around the coats of the blood-vessels (Fig. 5).

They are very rare tumours, but an interesting thing about them is this: In the ordinary way, if there had been no such thing as microscopic pathology this tumour would have been termed a "medullary cancer."

These tumours are moderately malignant, many are benign. So we were able to assure the patient's friends that although it was necessary to remove the breast with the tumour the prognosis appeared to be good.

Now, a thing which will be very interesting to you when you come to study these things in the out-patient department is this: A certain number of cases will come under observation in which the youngest dresser will have no difficulty in saying it is cancer, yet there are also cases in which, if you ask half-a-dozen surgeons to see the case, three will take one side and three another in regard to their opinions as to whether the lump in the breast is malignant or not. However, we are beginning to understand these matters, and the rule with surgeons in regard to tumours in the breast is this: when a woman has a lump in her breast which has the ordinary physical characters and signs of carcinoma, it is the wisest thing, particularly if she be over thirty-five years of age, to advise her to have the breast removed while the disease is in the early stage. Never advise the patient to keep under observation, and smear the breast with belladonna or some other messy and disagreeable pharmacopœial preparation, whilst you "watch" the case. Doctors used to watch six, eight, nine months or a year, and by that time the breast had enlarged and begun to ulcerate, and then, when they arrived at the certainty that it was cancer, the disease was quite beyond the reach of helpful surgery. Directly you get a patient who has a suspicious lump in the breast, especially if she is over thirty-five years of age, then, not only for the patient's peace of mind but also for the welfare of her body, advise her to have the whole breast and the axillary lymph-glands extirpated.

THE NATURAL HISTORY OF CANCER OF THE BREAST.

III.

CANCER of the breast has been known for centuries ; the part is so open to observation ; it is, indeed, the organ from which we derived primarily all our knowledge of the course, structure, treatment and termination of cancer. The interesting thing with regard to cancer of the breast is this : it is not a vital organ, and therefore when it is the seat of cancer you can watch the course of the disease in its purest form. You will remember that when we were talking about the general characters of cancer, its microscopical features and its mode of spread, I was anxious to point out to you that the cancer itself, the primary focus, cannot be regarded as a rapidly fatal disease ; cancer itself is dangerous and fatal on account of the peculiar way in which it disseminates, and especially from the method in which it lays the patient open to septic infection. The effects of the primary disease can be studied better from cancer of the breast than in any other organ, and some persons are averse to having anything to do with doctors (even years before Christian Science was invented) and look upon them as malicious people, and keep carefully away from them until the disease becomes inoperable. It is in these patients that you can study the natural history, so to speak, of cancer : some of them are very interesting to study because I shall try to show you that the primary growth sometimes

undergoes spontaneous cure. This is a matter of very great interest, because there are many surgeons who look upon cancer as a parasitic disease ; indeed it may be compared in many ways with syphilis, which, as you know, starts from a primary sore or ulcer, and in the course of a certain number of weeks, whether the sore is treated or not, it heals, and is replaced by a well-marked scar, which persists throughout the patient's life. Although the primary sore heals the system becomes infected, and later on a number of secondary lumps develop in the tissues and organs of the body which are known as gummata. In many ways cancer approaches nearer to syphilis as an infective disease than any other. The great point of difference between them is this : that in the case of syphilis the disease in remote organs, the gummatous lumps, are not produced by the transference of any tissue particles from the seat of the disease, but it is an active infective agent, the *Spirochæta pallida*, which produces it. Therefore all the tumours, wherever the lesion of syphilis occurs, whether it be on the tip of the nose or the tip of the penis, the finger or the buttock, the secondary lesions in the patient's body will be precisely the same ; whereas in the case of carcinoma, the secondary lumps which form in the body agree in character with the structure of the tissues in which the primary growth arose, and therefore vary in individual cases according to the nature of the organ in which the cancer originated. It is rare for the primary focus of cancer, particularly as far as the breast is concerned, to be the direct cause of death ; it is the secondary results which arise from that primary focus which produce such disastrous consequences to the individual. In order to show you how long some of these cases of cancer will run, I may mention that there are many carefully authenticated cases in which women have lived for twenty years with slowly progressive

cancer of the breast. This form of the disease is known as atrophic or withering cancer of the breast, and although it slowly destroys the nipple and the underlying glandular tissue, and progresses for ten, fifteen, or twenty years, the ulcer does not get any larger. The breast is continually shrinking away, and even both breasts may be destroyed. Then an inter-current malady, like pneumonia, or some form of lung trouble, will carry the patient off. There is nothing so striking as to see the patients in the wards and notice the slow way in which this form of cancer grows and causes them very little inconvenience, no pain, and they are able to enjoy life. Every now and then a patient will come to you, when she has heard of the death of some friend from cancer, and in the most confidential way tell that she has had an ulcer of the breast for five or six or eight years, and that she thinks it is time it was attended to. You do nothing for these patients; operation is not required for them, and they will live a very long time. But the ulcer never disappears; it is always slowly progressing and slowly shrinking the breast up, and it is as surely destroying also the tissues around. Unfortunately, however, all cases of carcinoma do not run this slow course. The younger the patient the more rapidly the disease grows and disseminates. As far as I know, cancer of the breast has never been recorded in a patient younger than fifteen years of age. There are very few cases of cancer of the breast recorded before the age of twenty-five. The majority of the patients are between thirty-five and fifty years of age: it is in these fifteen years that the larger proportion of breast cases come under observation. Cancer of the breast has been observed in women ninety years of age. The worst condition under which we meet with cancer of the breast is in women who are suckling. It does sometimes happen that a patient with cancer of the breast becomes pregnant; then it grows

with tremendous rapidity; such cases are referred to in text-books of surgery as acute scirrhus, and the skin of the breast is quickly involved, the lymph-glands are infected, and the patient dies very rapidly from dissemination of the disease.

Cancers are badly supplied with blood, but they are very rich in lymphatics. The breast, like other cutaneous organs, is very abundantly supplied with lymphatics which communicate with the lymph-glands in the axilla and in the mediastinum: there is also a rich plexus of lymphatics permeating the whole of the fascia which covers the body. When a breast becomes cancerous the infective cells implicate the lymph-vessel, and the lymph-glands first affected will depend on the position in the breast of the primary focus of the disease. When the cancer affects the breast at the base of the nipple the lymph-glands in the axilla are soon infected; when the cancerous focus is on the sternal side of the nipple, and particularly in what is spoken of as the sternal process of the breast, then the cancerous material finds its way into the lymph-glands which lie in the mediastinum. They will pass along the lymphatics which pierce the intercostals near the border of the sternum. The mode by which the lymphatics are involved is of interest. It is not merely that the cancer-cells find their way into the lumen of the lymphatics and then float along like a cork on a stream, or like fishes in a pond. A striking feature of cancer is its power of invading and eroding any tissues with which it comes in contact: so great is its power of eroding living tissue that it will form large holes in bones, as the specimens in the museum testify. Cancer rarely invades the walls of arteries, but it quickly implicates the thin walls of veins and lymphatics, and in well-marked conditions the tissues of these vessels will be replaced, and their lumina obliterated by a solid cord of cancer.

We must now consider the effects on the lymph-glands. If you make an ordinary examination of the axilla in the operating theatre you will find the lymph-glands in the normal way quite small, very little larger than a pin-head; but when infected with cancer they may rival chestnuts in size and form a large bunch in the axilla, which, in the latter stages, may be as big as a fist. When the lymph-glands enlarge they are in the early stages easily separable from each other, but in the later stages they may become so stuffed with cancerous material that the capsules burst and the glands form a conglomerate mass. The limits of individual glands are usually destroyed, and then the cancer implicates the skin of the axilla and ends in ulceration, and the ulcerating primary focus in the breast and lymphatic mass in the axilla tend to fuse together and after sloughing leave an unsightly hole; on its floor, in advanced cases, you will see the axillary vessels pulsating. In some cases the axillary vein is broached by the ulceration, and the patient will bleed to death. It is an easy ending, for when these patients are slowly bleeding to death they will say they never felt so comfortable during the whole course of their disease. I am sure it is no use trying to prolong their lives by permitting an energetic house-surgeon to apply a ligature to the subclavian artery.

There are other ways in which cancer victims die. After the lymph-glands in the axilla have become plugged with growth, the infection extends above the clavicle to the supra-clavicular glands; this leads to infection of the thoracic, or the right lymphatic duct, according to the side affected, and the cancer material finds its way easily into the blood and is distributed to the lungs. When the lymphatics lying in the mediastinum become infected, as they often do, the patient experiences respiratory difficulties, because the enlarged mediastinal glands press upon the trachea.

A fair proportion of patients with cancer of the breast die from suffocation owing to the pressure of enlarged lymph-glands on the trachea. While the lymph-glands are enlarging, permeation is going on in the case of the minute lymphatics in the fascia, which covers the thorax and the abdomen. You will be surprised sometimes in the *post-mortem* room, when you see bodies of patients who die from cancer examined, to find large secondary masses in the liver, ovaries and omentum. It was thought for years that this infection of the liver and of the ovaries was due to transportation of cancer-cells from the primary focus by means of the blood-stream into these distant abdominal organs. Mr. Handley has investigated this matter. He teaches us that this infection of the abdomen occurs in a very insidious way. The cancer material finds its way along the lymphatics underlying the fascia of the trunk and makes its way towards the epigastrium, where a number of fibrous structures come into relation; for example, there is the fascia, which overlies the body generally, immediately beneath the fat; the linea alba, where the abdominal muscles meet; the sheath of the rectus and all the aponeuroses connected with the abdominal muscles. Mr. Handley has shown that in chronic cases the cancer-cells permeate the lymphatics, travel down the fascia to the epigastrium and pass down the round ligament to the umbilicus; thus the whole of these soft tissues become infiltrated with cancer-cells. They then infect the lymphatic plexus lying in relation with the peritoneum, and the cancer-cells fall into the general cavity of the abdomen; they drop on the liver and omentum, take root and grow into secondary masses. The peritoneum always contains a certain amount of fluid or lymph, and these cancer-cells get into the peritoneal fluid and are conveyed by it into the recesses of the pelvis and lodge on the ovaries and the vascular uterus, and grow into big

cancerous masses. It seems as if the ovary is particularly favourable for the growth of cancer-cells, for I have found it on several occasions converted into a mass as big as a cocoa-nut.

In cases of epigastric invasion, I have seen the umbilicus well retracted by cancer growing in the tissues associated with the round ligament of the liver and resembling a retracted nipple.

Many patients with cancer of the breast die from this epigastric invasion; the proportion varies from 15 to 20 per cent. Indeed, Mr. Handley goes so far as to say that this epigastric invasion is so common that it should be our duty, when we examine a patient to see if she is fit to be submitted to excision of the breast for the cure of her cancer, to make a pelvic examination, so as to be sure that the pelvic organs are not infected; if they are it is useless removing the breast.

Patients suffer much when the skin covering the chest is invaded by cancer. Here is the picture of a patient who had her breast removed (Fig. 6). She had a recurrence in the skin, which in consequence is dotted with cancerous nodules and is hard like leather, or pig-skin. The condition is known as cancer *en cuirasse*. Whenever there is this peculiar condition of skin and the lymphatics of the axilla are blocked up, the arm is swollen. It is always an uncomfortable sign when a patient comes back with the arm and forearm cedematous. This goes on until the limb appears like an elephant's leg; it is so swollen and dense and hard that it can scarcely be impressed by the finger, and so heavy that it produces lateral curvature of the spine if the patient persists in walking about. At last the limb becomes so heavy that the woman is confined to bed. Some years ago it was the practice to take such arms off. I have amputated several for this condition, and in two instances I have even removed the scapula, and the

patients have been more comfortable in consequence. I have known a woman live two years after such an operation. Still, the condition of these patients is



FIG. 6.—Cancer *en cuirasse* with lymphatic œdema of the arm.
From a photograph.

very miserable. Mr. Handley, acting on his idea concerning the spread of cancer by means of the lymphatics, has devised and practised with success an operation by means of which he makes a new

lymphatic channel. He introduces into the subcutaneous tissue a number of buried silk threads running from the wrist upwards to terminate in the loose areolar tissue over the scapula. These threads act like the wick of a candle, and drains the lymph back into the circulation ; it is much simpler than practising removal of the arm. I have seen several of the cases in which this procedure has been carried out, and the patients have been very comfortable.

Another way in which women die is when secondary cancer occurs in bone. We have always thought that cancer found its way into bone by the blood-vessels. We know now that it is mainly due to permeation. When a bone becomes permeated with cancer any slight effort will cause the bone to break, and cases have happened in the cancer ward where a patient raised her hand to scratch the back of her head, even this slight effort has caused the clavicle to break ; or she may be arranging the pillows and break the humerus, or in trying to get out of bed, or scratching one foot with the other, she will break her thigh-bone. This is called spontaneous fracture, and although these bones are permeated with cancer, if they be kept in apposition by splint and bandage in the same way as in fractures from other causes union often occurs.

Deposits of cancer in long bones rarely attain a great size, and although they entail strict confinement to bed they do not often produce pain. But there is a condition in which cancer in bones produces agonising pain, and that is when there is a deposition in the vertebræ. The pressure of a cancerous mass on the roots of the nerves, or on the nerve-trunks as they issue from the intervertebral foramina produces most agonising pain. This is a practical point to remember, because sometimes old ladies who have cancer hidden away in their breast, which they do not like anyone to see, will consult you

on account of pain in their legs. Whenever you are called to such a case and you do not find anything to account for the symptoms, always carefully examine the breasts. In a certain number of such cases you will find a cancerous knot of which the patient is totally ignorant; sometimes they admit that the knot has been in the breast several years; of course they cannot think of any connection between the lump in the breast and the pain in the back. When these women become paraplegic there is no operation which can be done for them; they get troubled with bladder symptoms, the sphincters are paralysed, and they die from uræmia due to septic pyelitis.

We treat cases of cancer by operation in the belief that it is a local disease. Later on, when you have time to read the history of these things, you will be interested in the accounts of the cancer discussions of thirty years ago, when the greatest surgeons, physicians and pathologists of that period argued whether cancer was a constitutional or a local disease. To-day the idea that it is a local disease prevails, and the way to cure it is to remove it if there are no signs of dissemination, or wide implication of skin or enlarged supraclavicular lymph-glands. But do not run away with the idea that all the cases you operate upon are going to be cured. Some of those cases are made very much worse by operation, and I tell you why. We do not know the limitations of cancer; it lacks a capsule, and when you take a cancerous breast and divide it with a knife you cannot define its boundaries. For this reason the surgeon takes away the whole breast even when the cancer is no bigger than a cherry. If the disease has been in existence some time, and the lymphatics are permeated with cancer, in removing the breast and opening up the axilla fresh tissues are freely exposed, and in squeezing the lymph-glands during the operation cancerous material is forced out and accidentally

spread about the wound area; the surgeon practically sows this freshly prepared ground with cancer-cells, and they will grow. Occasionally the patient comes back a few months later with the whole operation area infiltrated and hard with cancer. As a matter of fact in such cases the surgeon has produced a fresh condition of cancer, known as post-operative cancer infection, and there is no doubt that in some instances, where operations have been performed clumsily, and even sometimes when they have been performed with great skill, but particularly when they have been done roughly, the disease becomes much more extensive than before the operation was performed. We do our best. Some of our patients do remarkably well, some are no better off after operation than if the disease had been left to run its own course. However thoroughly or early in the course of the disease the breast is removed no prophecy can be made as to the future of the patient; no amount of microscopical examination of the tissues will enable you to make a forecast. In many cases which look clinically unpromising the after-events have proved good, and on the other hand some cases which seemed to promise favourably have turned out badly.

There is yet another way in which these cases die. Cancer implicates the chest wall and permeates the intercostal muscles and infects the pleura; then the patient gets bronchitis and septic pneumonia, and pleurisy, and other chest complications which terminate fatally.

The one lesson I want you to take away is this: it is not so much the primary focus of cancer which destroys life as its power of dissemination, and the remarkable vitality and power possessed by cancerous cells to grow in any tissue of the body, whether skin or bone, brain or liver, retina or ovary, in addition to the readiness with which cancerous tissue becomes septic.

CANCER OF THE GASTRO-INTESTINAL TRACT.

IV.

CANCER of the alimentary canal destroys life much more rapidly than when it attacks the breast. A study of this matter affords an impressive illustration of the effects of environment in connection with this disease. The whole of this subject is extremely interesting and important, because more than half the total number of cases of cancer arise in connection with the alimentary canal. If you take independent organs of the body and compare the stomach in this regard with the breast and the uterus, these three situations prove to be the most common in which cancer arises. For my own part I think the order in which they stand in this respect is that cancer of the breast is the commonest, whilst cancer of the uterus and cancer of the stomach are of equal frequency. But some writers who have paid great attention to the statistics of this matter are of opinion that cancer of the stomach is commoner than cancer of the breast, or of the uterus. This is striking enough, but if the whole of the alimentary tract from the œsophagus to the anus is considered, we find that more than half the cases of cancer originate in it.

The distribution of cancer in the alimentary canal is important, for it is common in the œsophagus, frequent in the stomach, rare in the small intestine, uncommon at the ileo-cæcal valve, but very common in the large bowel and rectum. These facts are of great

interest to those who are working at the origin of cancer, because the frequency with which cancer attacks the large intestine is in favour of those who believe that cancer is due to a micro-parasite, probably something which is taken in with uncooked food or with water. Indeed I feel so strongly on this matter that for many years I have avoided eating all sorts of uncooked vegetables. Much as I enjoy salad with my chicken, or my cheese I do not touch it. I do not wish to prejudice you against the delights of the table, but I think these facts are worth bearing in mind: however clean your celery may appear to be, if you pull aside the stalks immediately around the centre of the celery, which is about the only part worth eating, you will see that there remains some dirt which has not been washed away. In regard to the preparation of uncooked vegetables for the table I think it well to draw your attention to the remarks of a Frenchman visiting England. He said, "You English are remarkable people; you live well and like to eat vegetables, but it is the only country in the world where the scullery-maid is trusted to prepare the vegetables." There is much truth in this remark.

Some years ago, when I made almost daily visits to the Zoological Gardens for the purpose of making post-mortem examinations of the bodies of animals dying in the menagerie, the extreme frequency with which their viscera were invaded with parasitic worms was a matter of great surprise to me, and they were often present in uncountable numbers. On contemplating such things one felt deeply thankful that most of the food eaten by mankind is cooked. We know full well that living on partially cooked or "under-done" meat carries penalties in the way of Entozoa, as the intestinal parasitic worms are called.

Some years ago I operated on a patient for appendicitis, and in the early stages of the disease she

suffered from persistent diarrhœa. To relieve this she had taken for several days a quantity of raw pounded beef on the advice of her doctor. As a consequence she suffered severely from an acute infection of beef tape-worms (*Tænia mediocanellata*). Events of this kind make us agree with Metchnikoff that "Entozoa may serve as gates of entry for the hypothetical parasites of carcinoma." There are many channels by which minute but not invisible Invertebrata gain an entrance into the alimentary canal. Food and water are essential to life, and it is undeniable that they are the frequent purveyors of disease, and that minute animal parasites are our daily messmates and table companions, though their presence we sublimely ignore.

To return to uncooked vegetables. One of the most striking observations relating to this matter we owe to Behla concerning the town of Luckau in Germany. This town contained 5000 inhabitants, and the majority were engaged in agriculture. Between the years 1875-1898 the death-rate from cancer was very high, and numbered one out of twenty-five to thirty for the entire town. The cancer cases, however, did not arise in all parts of the town. More than half the population inhabited its central portion and the eastern suburb, where the houses were similar in size and arrangements, and, as a rule, damp. The soil of these parts of the town was moist and lay low. A large ditch encircled the central town and the eastern suburb; the cancer followed closely the course of this ditch, which contained foul and stagnant water, and in which the people watered and washed their vegetables, many of which were eaten raw. The western suburb was sandy, dry and elevated, and remote from the ditch. In this part of the town there was not a single death from cancer during the period investigated by Behla.

In Behla's opinion the probable vehicle of infection was the uncooked vegetables.

Behla believes that it is proved by observation that cancer is due to a micro-parasite, and that it is a vegetable organism which enters the blood through skin or mucous membrane; its spores penetrate epithelial cells and cause enlargement of their nuclei and asymmetrical mitoses, and later they produce proliferative irritation. Finally a sporangium is found within the cell, or close to it, in the infected tissues. As these parasites have not yet been cultivated experimentally the cause of cancer still remains, like that of smallpox, in the domain of hypothesis, although, be it remembered, there are several very infectious diseases of which the parasite has not been detected, much less cultivated, and yet the infectivity of the disease is beyond dispute.

Let me draw your attention to the unequal distribution of cancer in the alimentary canal.

The œsophagus.—Compared with the other parts of the alimentary canal the mucous membrane of the gullet is not very vulnerable to cancer. It is more common in advanced life, and may be described as rare before the fortieth year. Any part of the œsophageal mucous membrane may be attacked, but it is more common in the upper than in the lower half. Carcinoma of the gastric end of the gullet is uncommon. This I thought might be due to some difference in the method of tabulating the cases, for it seemed possible that in some statistical tables cancer at this end of the œsophagus might be tabulated as belonging to the stomach. This is correct, but even including such cases it is true that cancer around the terminal orifice of the gullet is uncommon: nothing is known of its early stages in this situation, for it produces no symptoms until the œsophagus is narrowed and hinders deglutition. As soon as the cancer is revealed in this way its course is very rapid. The patients die from inanition and exhaustion from obstruction to the passage of

food, pleurisy and septic pneumonia. Death also occurs from hæmorrhage when the cancerous ulceration opens up large vessels in the mediastinum, especially the aorta.

The stomach.—According to some statistical researches cancer arises in the stomach more frequently than in any other organ, and it is especially common in the parts lying along the lesser curvature and in the vicinity of the pylorus. This is a noteworthy fact, because this area may be described as the chief district frequented by ulcers. This is a matter of great interest, because many surgeons hold the opinion very strongly that cancer is prone to attack chronic gastric ulcers and the scars which they leave in healing. This is only in accord with the habits of cancer in other parts of the body, namely, it attacks by preference chronically diseased organs and tissues. In this respect a chronic gastric ulcer may be considered as a pre-cancerous condition. Gastric cancer runs, as a rule, a rapid course. Life is rarely prolonged beyond twelve months from the time the disease is first recognised. This quickly fatal course, especially when the pylorus is implicated, depends largely on the obstruction offered to the escape of the chyle from the stomach into the duodenum. Death may be due to slow starvation, hæmorrhage, perforation into the general peritoneal cavity, septic pleurisy from perforation of the diaphragm, general dissemination and thrombosis.

The small intestine.—Primary cancer of the small intestine is rare; the common segment in which it arises is in the second part of the duodenum, at or near the bile papilla. The next point is at the ileo-cæcal valve, but here the disease is uncommon, especially if care be taken to distinguish between cancer arising in connection with the valve and cancer originating in the mucous membrane of the cæcum.

The large intestine and rectum.—Primary cancer of

the large intestine is a common disease, and the liability of its mucous membrane to become cancerous increases from the cæcum to the rectum. Thus cancer is thrice as common in the terminal two feet of the large gut (sigmoid flexure and rectum) than in the remainder of the colon, and if care be taken to discriminate between hyperplastic tuberculous disease of the bowel and cancer the disproportion will be found even greater.

Of the initial and early stages of cancer of the colon we know nothing; the disease has no special symptomatology, and causes no pain until it has so narrowed the lumen of the gut that the intestinal contents (fæces) are hindered from passing; then the patient suffers from intestinal obstruction, and seeks advice, and, in many instances, when the cancer reaches this stage, unless surgical help is quickly forthcoming, the patient will succumb from perforation of the cæcum, or the colon above the stricture.

The character of the disease in the early stages is unknown, for it grows unsuspected and unrecognised, and in an absolutely painless manner until the lumen of the colon is too narrow to allow fæces to pass, then pain is the sequence; even then the disease remains undetected often for many months. In the colon cancer appears in its final stages in two forms. It may be massive and exuberant, the cancerous mass blocking up the bowel. The other form is the more insidious, for the cancerous growth may resemble the small contracting nodule so often present in the breast. When cancer attacks the colon it spreads around it in a circular manner; in the contracting form it will narrow its lumen until the colon appears as if a piece of cord had been tied tightly around it.

I have long held the opinion that in these extreme contracting forms of cancer of the gut we have, as I endeavoured to explain to you in connection with the

small contracting forms of cancer in the breast, examples of a primary cancer undergoing spontaneous cure. Here, of course, the cure is almost worse than the disease, for this very complete cicatricial contraction of the primary growth leads to the very condition which renders colic cancer such a rapidly fatal disease, namely, obstruction of the intestine.

A comparison of cancer of the breast and of the gastro-intestinal tract is useful in another way. Mammary cancer is a chronic disease and dissemination (metastasis) is the rule. In the stomach and large bowel cancer usually runs its fatal course quickly, and dissemination is unusual; nevertheless secondary deposits are seen in patients affected with gastric, colic, or rectal cancer when the disease is chronic. The following case reported to a society some years ago illustrates this point, and indicates the insidiousness of colic cancer. A woman had a tumour as big as her head growing from the shaft of the humerus. It was regarded as a periosteal sarcoma. The limb was amputated at the shoulder-joint. When examined microscopically this tumour contained spaces lined with tall columnar epithelium; it also contained lymphoid follicles like those which normally occupy the rectum. The patient was carefully examined and a cancer was found growing in the rectum.

In 1906 I reported some similar cases in which large bilateral tumours replacing the ovaries were removed, but in the course of the operation a primary cancer was found in the gastro-intestinal tract. The tumours in the ovaries contained glands derived from the cancerous epithelium in the intestine ('Brit. Med. Journ.,' 1906, i, 1216).

When cancer arises in the rectum we find an additional element of danger, because the cancerous mass is in close proximity to the bladder and the ureters. In the late stages of the disease these organs become

involved, and, apart from the extreme misery produced by the formation of urinary fistulæ, the patient's life is terminated by septic invasion of the urinary system, which leads to death by uræmia.

The comparison of cancer of the breast and cancer of the gastro-intestinal tract in relation to its life-destroying properties is extremely instructive. As we saw in a former lecture, cancer, when it attacks the breast, runs an insidious course, and only a small proportion of its victims die from the direct result of the primary disease, whereas when cancer attacks the stomach and large intestine primarily it so profoundly interferes either with alimentation, or with the escape of the gross excrementitious products of the body, that life soon becomes impossible. Thus from the practical side of our work it is incumbent on all to keep themselves thoroughly informed of these variations in the clinical behaviour of cancer in these different situations.

From the scientific point of view the liability, or better, the vulnerability of the various sections of the alimentary canal to cancer is most instructive in relation to its ætiology. For example, those parts of the digestive tube are most prone to become cancerous where food makes the longest sojourn. The œsophagus is merely a conduit, or food duct. The stomach is a churn, and in this hollow viscus there is much mixing and motion of the ingested material, and therefore prolonged and close contact. The digested mass is hurried through the small bowel into the cæcum, where it is retained for many hours and is ordinarily deprived of the main part of its fluid. That the undigested residue known as fæces is retained for many hours, and in some ill-conditioned individuals for days, in the descending colon and sigmoid is an undeniable fact.

This retention would be favourable for the invasion of the epithelial covering of the gut by an infective agent.

Primary cancer of the stomach, cæcum and colon appeals to those who are interested in the clinical recognition of this disease, on account of the difficulties which so constantly arise in the diagnosis of cancerous affections of the gastro-intestinal tract. Cancer has no "specific symptomatology." This is no mere catch-phrase; it is a reality. A patient accidentally feels a lump in the belly and seeks advice; in many instances an astute physician or a practical surgeon with wide experience will have little trouble of coming to the conclusion that a given lump is "malignant." If the lump lies in the upper half of the abdomen he will find some difficulty in deciding whether it be connected with the stomach, gall-bladder, liver or transverse colon. A cancerous gall-bladder will sometimes involve all these structures.

When the lump is situated in the right flank, diagnostic obscurity is somewhat less, but the wisest and most experienced are greatly puzzled to decide between primary cancer arising in the cæcum, and chronic inflammatory affections starting in the vermiform appendix.

Primary cancer in the sigmoid flexure of the colon does not often cause doubt in diagnosis, but when a cancerous lump in this segment of the colon drops into and lodges on the floor of the pelvis, it is apt, in a woman, to be mistaken for an enlarged ovary or Fallopian tube. This is a common error in gynecological diagnosis. It is also useful to remember that in middle-aged and elderly women the transverse colon sometimes forms a wide omega-loop, and if a cancerous lump forms in the lowest segment of this curved piece of colon it will drag it down to the pelvis. I have seen the fundus of the uterus so implicated in this way that in the course of an operation it was impossible to decide whether the primary focus arose in the uterus or in the transverse colon. It is by no means uncommon

when investigating, in the course of an operation, a suspected malignant mass in the neighbourhood of the umbilicus, to find the stomach and transverse colon so implicated as to leave it doubtful whether the primary focus arose in the stomach and involved the transverse colon, or *vice-versâ*.

In order to show how surgeons are hampered by this absence of a specific symptomatology for cancerous affections, it is necessary to mention that when a suspected cancerous mass connected with the gastrointestinal tract is exposed in the course of an operation, eyes and fingers are often incompetent to determine for, or against, malignancy. Hardness, indefiniteness, age of patient, enlargement of the adjacent lymph-glands, may all deceive. Even microscopic investigation of the tumour itself may fail. It is only necessary to read reports of cases published by reliable and conscientious surgeons to learn, that severe operations have been performed under the impression that the disease was cancerous; subsequently a careful microscopic examination has proved the mass to be of inflammatory origin, and this opinion has been justified by the complete and permanent recovery of the patient. It may be useful to tell of some of these difficulties: In 1906 a woman, aged thirty-three years, was admitted into the hospital under my care with a movable lump as big as a muffin in the epigastrium. She complained of frequent vomiting, especially after taking a meal. The patient was emaciated, very ill, and in pain. I had no doubt that the lump belonged to the stomach and most probably was cancerous. On exposing the stomach in the course of the operation a large saddle-shaped mass could be seen involving the parts about the lesser curvature. The stomach being movable and the growth confined to the gastric tissues I was able to remove nearly the whole organ (gastrectomy). After removal, the tumour mass was made the subject

of a careful histologic examination in the clinical laboratory and in the Cancer Investigation Department. Each investigator reported the growth to be cancerous. I critically examined the sections and dissented from the opinions of my histological colleagues. A fresh set of sections were prepared and examined with the same results.

Three years passed away and the patient remained in good health; her only complaint is that she has to take her meals more often and in smaller quantity than is the case with her neighbours who possess stomachs of normal size. I feel justified in assuming that the post-operative course of this patient justified my opinion that the thickening of the walls of her stomach which led me to extirpate the organ was inflammatory, not of cancerous origin.

Since gastro-jejunostomy has been freely practised for the relief of obstructive affections in the pyloric region, believed to be cancerous by physicians in charge of the patients and the handicraftsmen who performed the operation, they have been astonished on seeing the patient some months later to find that the suspected cancerous lumps have disappeared. Facts of this kind may be gleaned from the records of almost any general hospital in London.

A localised thickening sometimes arises in the walls of the intestine, especially the cæcum and colon, which is extremely liable to be mistaken for cancer, and to which Hartmann has recently directed our attention, namely hyperplastic tuberculous disease. To the ordinary clinical methods and even on visual examination it is often very difficult to distinguish between this affection and primary cancer, but happily the distinction is easily made on microscopical examination, the presence of the multinuclear (giant) cells furnishing an easy means of identification.

Every surgeon of experience can recall instances in

which he has felt convinced on examining a hard, indefinitely circumscribed swelling in some region of the abdomen that it depended on cancerous disease of the large bowel, and regarded the case as inoperable and hopeless ; finally an abscess has burst spontaneously either into the bowel, or externally, and the patient has slowly recovered. Unfortunately the converse of this is true, for a patient may have a cancerous lump of moderate dimensions growing from any part of the large bowel, but especially in the neighbourhood of the cæcum, the hepatic or the splenic flexure ; such lumps are particularly liable to septic infection, as the cæcal and colic segments of the intestinal canal abound in pathogenic micro-organisms. This leads to ulceration and often perforation of the bowel, which permits leakage of the intestinal contents and the formation of an abscess. It occasionally happens that the surgeon evacuates pus associated with a primary colic cancer under the impression that he is dealing with a peri-colic abscess, and gives the patient satisfactory assurances ; but the relief is temporary and a fistula discharging faecal matter persists. Eventually the chronic course of the case leads to a more thorough investigation of the sinus and the unpleasant discovery of its dependence on a primary but septic cancer.

To show further how chronic inflammatory thickenings of the large bowel mimic in their clinical features colic cancer, and how cancer of the colon which is thoroughly septic simulates chronic peri-colitis, it is necessary to mention that foreign bodies like pieces of straw, needles, small chips of metal, or a piece of whalebone accidentally introduced with food will perforate the bowel, or lodge in a colic diverticulum, or penetrate an epiploic appendage, and lead to local thickening of the bowel, which so strikingly resembles the clinical signs of cancer, in middle-aged and elderly persons, that colotomy and resections of the gut have been performed under

the impression that the disease was cancer. I published a series of cases illustrating this matter ('Lancet,' 1903, vol. ii, p. 1148).

In some instances where patients have been submitted to colotomy on account of intestinal obstruction supposed to be due to cancer of the colon, and had survived this operation several years, I have often thought there was fair probability that the obstruction did not depend on cancer. For several years I have made some critical observations on this matter, and found to my surprise that although in the majority of patients with cancer of the colon which has advanced to the stage which needs relief by means of colotomy, the average expectancy of life is eighteen months, some occasionally come under notice in which life has been prolonged four, five, and even seven years. Death in some of them has been due to secondary deposits in the liver, slow implication of the urinary organs, or thrombosis from septic infection of big veins arising from the permeating effects of the cancer at the primary focus.

Facts of this kind are full of interest, for they illustrate that even in the big bowel, where cancer is so easily liable to become septic, that if the gross mechanical effects can be overcome this disease may, and does in some instances, pursue a chronic course. From the therapeutic standpoint this is hopeful, for while the bacteriologist is at present helping to limit the dire results of septic poisoning, by means of prophylactic sera prepared from the pathogenic micro-organisms which happen to flourish in a particular cancer, we are all hopeful that some similar cunning fluid will be prepared, which, when injected into the circulation, shall cause the cancerous tissue to disappear in the same startling and often magical way in which diphtheritic membrane dissolves after the injection of the appropriate antitoxin.

VILLOUS DISEASE OF THE URINARY TRACT.

V.

A WOMAN, aged sixty-six years, was sent into Bird Ward to see me, and she brought in her hand demonstrative evidence of her disease in the shape of a bottle filled with bloody urine. This at once showed that she had some morbid condition of her bladder, ureters or kidneys. The most obvious thing to do was to examine the urine in order to be sure that its abnormal colour really depended on the presence of blood. It was of the colour of porter and contained a large amount of blood-corpuscles, but we found no evidence of epithelial cells. The patient was admitted, and in due course we proceeded to examine the interior of her bladder. The proper way to do this, either in the case of a man or of a woman, when you think there is any serious disease of the bladder, is to inspect its interior by means of the cystoscope. The old-fashioned way of examining the bladder of females, when we wished to know if there was anything wrong inside, whether a tumour or a hairpin, or a calculus, or a bodkin, consisted in dilating the urethra and introducing the forefinger. It was a rough and ready way, but one which was very useful. When the urine is blood-stained the cystoscope will not light up the bladder, and you may wash out the blood-stained fluid, and often the more you wash it out the more the bleeding goes on. Therefore, to examine this woman's bladder by the cystoscope was out of the question, so I dilated

the urethra and put in my finger, and was able to feel two small tufts of what is known as villous disease, or papilloma. Sometimes when these villi are not bleeding it is possible to gently fill the bladder with water and watch them by means of the cystoscope. When this is done skilfully they appear as beautiful objects; these villous tufts are of a light pink, looking very much like anemones when seen in the illuminated tanks of an aquarium. These papillomata arise from the vesical mucous membrane, and there may be one or many tufts in the bladder. When examined microscopically they have a very characteristic structure. They consist of an axis of delicate connective tissue containing blood-vessels, and over this, on a basement membrane, you will see a cap of epithelial cells of the same character as those which line the interior of the bladder. The villous tufts are very vascular, and if from any cause their cells are detached, the blood-vessels, which form the axis of the villous tufts, begin to bleed, and sometimes, if a tuft be near the urethra, it may be long enough to be carried into this passage during the act of micturition, block it up and cause great pain—almost as much pain as when a stone is impacted in the urethra. Papillomata are particularly apt to grow near the vesical orifices of the ureters. It is an unpleasant thing in regard to these villous papillomata that they very often become malignant, and sometimes in that particular portion of the bladder from which the villous disease grows the cells take on malignant action and penetrate the bladder-wall. Indeed, some surgeons who devote their attention to the bladder, prefer, unless these papillomata are causing great trouble, to let them alone, because they are of opinion that by detaching them you injure the integrity of the mucous membrane of the bladder, and changes may be set up which end in malignancy.

My own experience teaches me to regard a villous papilloma as a pre-cancerous condition, but, as in other conditions of this kind, they may exist for many years and never become cancerous. Many years ago, when acting as a dresser, I remember well an old man who had been at intervals in the hospital over a period of seventeen years on account of hæmaturia, which was regarded — and correctly — as being due to villous disease, because when he came in with these attacks we used to find fragments of the villi in his urine, so large that they did not require any magnifying glass to see them. About that time (1880) it became the custom to remove vesical papillomata through an incision made in the perinæum. This man was subjected to the operation and he died in consequence. His bladder (which is preserved in the museum) contained a large tuft of villous papilloma. Another very remarkable thing about these cells on the tufts of the villi is their vitality. Those of you who are interested in the cytology of malignant growths cannot do better than examine the epithelial cells that lie on the top of these villi. They show mitotic changes in a very remarkable manner, and they also illustrate in a very striking way the power which these cells have of engrafting themselves on to the tissue with which they come in contact.

The pelvis of the kidney is lined with epithelium, and from this villous papillomata may grow like those which grow in the bladder. Our museum contains two admirable examples. As in the case of the bladder these villous tufts are often detached, and the fragments are conveyed down the ureter by the urine, and in their passage they cause pain and distress exactly like that produced by a calculus when it passes down the ureter. They are not common, but a fair number of cases are known, and kidneys have even been removed because of them. Some enterprising

surgeons, when they have opened the kidney and found its pelvis full of villous tufts, removed the papillomata, and saved the kidney. Such efforts of conservative surgery have been rewarded with success. But these villi in the kidney are also interesting from another point of view. Dr. Murchison, a very distinguished physician, who at one time was on the staff of this hospital, found in the course of a *post-mortem* examination a kidney with its pelvis stuffed with villous papillomata; some similar tufts grew from the vesical mucous membrane near the orifice of the ureter. Murchison believed that these were due to cells which had descended the ureter with the urine, and had engrafted themselves on the mucous membrane of the bladder.

Now to finish with the case of the old lady. We took her into the theatre, and discovered that she had papillomata in her bladder, and with the assistance of Sim's speculum I opened the bladder through its posterior wall and removed the villous tufts. After removing the tufts we sewed the bladder up, and the house-surgeon and myself were particularly anxious to see the condition of the urine next morning, and to our satisfaction we found the urine free from blood.

Let us pass from these papillomata with rich epithelium, which grow in the bladder and in the kidney, to another extremely interesting kind of villous papillomata, namely, those which grow in the interior of cysts in the immediate neighbourhood of the ovary. There is a certain kind of cyst which grows between the layers of the mesosalpinx which is extremely prone to have papillomata on its inner surface: these warts may occur here and there, or they may form definite clumps, which sometimes become calcified, or they may form huge dendritic masses inside the cyst until, merely by their power of growth, they burst the cyst open, and then you see the whole of that surface

which the cyst formerly occupied replaced by a thing which looks like a cauliflower.

The papillomata in these cysts are vascular, though perhaps not quite so vascular as the vesical papillomata, and when the cyst is ruptured the movements of the intestines detach cells from the warts they contain and strew them over the pelvic peritoneum and the surface of the bowels and in the recesses of the peritoneum, on which they engraft themselves and grow into papillomata. Crops of peritoneal warts of this kind are always accompanied by a large amount of free fluid in the abdomen. When such papillomatous cysts are removed the fluid does not reaccumulate and the warts on the peritoneum atrophy.

I have mentioned this matter in order to demonstrate the extreme vitality of epithelial cells. This leads me to consider that most remarkable and most vital of all cells known as the ovum or sex cell. The ovum may be practically regarded as an epithelial cell shed from an ovarian follicle. It is a large cell surrounded by a number of smaller cells in the ovarian follicle, and the ovum itself is derived from the cells which cover the embryonic ovary. These cells may, with propriety, be termed reproductive epithelium. Subsequently these reproductive cells, or ova, become embedded in the connective tissue (stroma) of the ovary. The sex cell, or ovum, is an epithelial cell. We began this lecture by contemplating a bottle of dirty urine, and by tracing its causes we find ourselves face to face with the great problem of life, which centres around the ovum.

CHORION-EPITHELIOMA.

VI.

I CONCLUDED the last lecture by briefly referring to the sex cell or the ovum, which I described to you as probably the most remarkable epithelial cell in the body. To-day I propose to give you some idea, from a pathological point of view, of its extraordinary character. Indeed, I will go so far as to say that the most wonderful thing that man ever found out about himself was when von Baer, in 1829, discovered the human ovum or egg, and thus established the nature of the ovary. Although we know absolutely that man, like all other animals, is developed from an egg, yet no one has ever seen a human egg fertilised, and no one knows anything about the changes which take place in that egg for the first fourteen days after fertilisation. All that we know about these changes is an inference from observation on the eggs or ova of birds, and some of the marine animals such as sea urchins and star fishes. After the egg leaves the ovary, if the environment be favourable, it may be fertilised and transformed into an *oöperm* or *zygote*. When we chance to meet the *oöperm* some fourteen or eighteen days later it presents a most extraordinary change, for not only has it increased enormously in size, but its investing membrane has become shaggy in consequence of the growth of those remarkable processes (Fig. 7), known as chorionic villi. In the early stage these villi grow over the whole of the external surface

of the chorion, but later they become collected towards one pole. In their early stages these chorionic villi are devoid of blood-vessels, and consist of an axis of delicate connective tissue covered with a layer of cells with definite cell boundaries, known by the name of Langhan's cells, and over this there is another cellular layer without definite cell boundaries, which looks like a large multinucleated cap of protoplasm lying on these cells. This is sometimes termed the syncytium. Em-



FIG. 7.—A human embryo of the sixth week, showing the polar congregation of the villi. (From the author's book on 'Diseases of Women.')

bryologists have named this epithelial cap the trophoblast, because by means of it the embryo derives nourishment from the maternal tissues. It is from these villous elements that the placenta is produced. Many years ago there was a most strenuous discussion carried on amongst the physiologists, and those who were interested in the development of the placenta, concerning the source of these two layers of cells. Some argued that the under-layer was derived from the foetal ectoderm, and the outer-layer came from the epi-

thelium which covers the decidua in the uterus. Many years ago, when I began to work at the pathology and the histology of tubal gestation, I satisfied myself that no decidua forms in the tube, and yet we find these two layers of epithelium on the chorionic villus. Therefore it is out of the question that they could have been derived from decidua. But so much work has been done on this question in recent years that there is no doubt in the minds of those whose opinion is most worthy of consideration that these two layers of cells are of foetal origin. At first the chorionic villi are avascular, but early they are vascularised through the intervention of an interesting organ known as the allantois, which later shrivels to a cord, except the part in relation with the cloaca, which becomes a receptacle for urine, and is known as the urinary bladder. So that Nature is as niggardly in bestowing rewards as the State in regard to old soldiers, for you may remember that they merely receive a small pension, which many eke out by looking after urinals and water-closets at railway stations and clubs. The chorionic villi grow with great rapidity, and embed themselves into any tissue with which they come in contact, and ultimately form that remarkable temporary organ which is known as the placenta. This is an organ which extracts, as you know, oxygen from the mother's blood in contact with these villi and converts the venous foetal blood into arterial blood; this in turn supplies the foetus with oxygen. And more than that, it is believed, and I think with truth, that these cells help the villi to extract a sort of pabulum from the blood, which is also used to nourish the foetus. With abstruse and physiological questions of this sort I am not concerned to-day, because I want to draw your attention to one of the most remarkable forms of tumour which affects the human body.

It has been discovered in recent years that these

cells are not only useful in that they form, as it were, a respiratory organ for the foetus whilst it is in the uterus, but they also possess a very powerful property by which they embed themselves in the maternal tissues. The trophoblast possesses the power of eroding or destroying any tissues with which it comes in contact. Cancer-cells have the same power. When the cancer-cell infects an organ and begins to grow it can erode and destroy healthy tissue with which

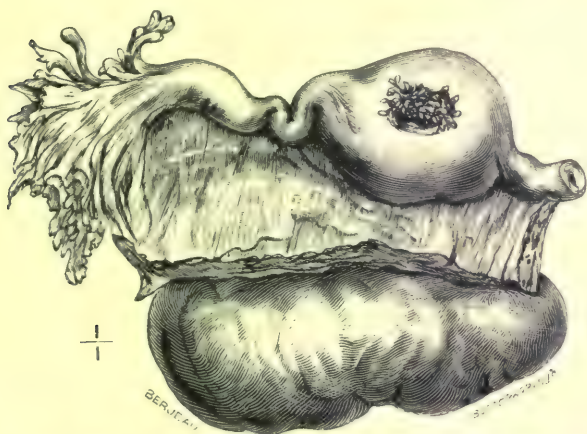


FIG. 8.—A gravid Fallopian tube and ovary. The chorionic villi eroded the walls of the gestation sac and caused fatal bleeding. (Museum of St. Bartholomew's Hospital.)

it comes in contact. Thus here in the trophoblastic tissue of the chorionic villi we have a physiological type of that erosive or invasive action of the cancer-cell. The manner in which the epithelium of the villi erode tissues and embed themselves into the underlying muscular tissue, is illustrated by the specimen represented in Fig. 8. It is a Fallopian tube and ovary obtained from a woman admitted into the hospital in the seventh month of her eighth pregnancy. After she had been in the ward a little time she was seized

with signs of internal hæmorrhage, and in something like eighteen hours she was dead. At the *post-mortem* examination a curious lump was found in the Fallopian tube, which was mistaken for malignant disease, and there is a small hole in the side of the tube through which some delicate processes protrude and float in the fluid in which the specimen is preserved. These

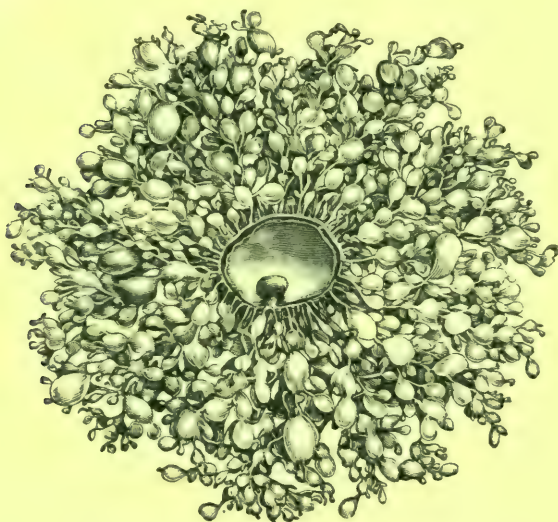


FIG. 9.—Hydatid mole. (After Bumm.)

floating processes are really chorionic villi. This woman had unfortunately conceived in the Fallopian tube as well as in the uterus, and when the ovum, or oöperm, as the fertilised egg is called, developed its chorionic villi, the activity of the trophoblast was so great that it eroded its way through the mucous membrane and the muscular wall of the tube, and some of the villi finally made their way through the serous coat into the general peritoneal cavity, causing the bleeding which destroyed the patient.

Under certain conditions, and we do not know what they are, these chorionic villi, instead of forming a healthy functional placenta, undergo a most remarkable change, and become transformed into a mass of things which looks like a collection of small grapes (Fig. 9). These chorionic villi undergo the peculiar change known as hydatidiform degeneration, because they look like the small vesicles which are such a characteristic feature of the disease which we call hydatids (echinococcus disease). Many years ago Virchow, who studied this disease, found that these grape-like bodies consisted of myxomatous tissue, and in structure resembled an ordinary nasal polypus, and it was then called colloid disease. Nobody troubled very much about hydatidiform disease of the placenta until it was discovered that women who were subject to it were often the victims of a curious form of malignant disease of the uterus which very quickly destroyed them. When the matter came to be investigated it was pointed out that these grape-like villi are not degenerations, but if you examine microscopically complete sections of the so-called vesicles, you find that although the centre of these grape-like bodies consists of more or less indifferent structureless tissue, yet their periphery is covered by a very active epithelium (Fig. 10), with here and there the peculiar bodies found in the decidua known as decidual cells. Later, cases were found in which hydatidiform vesicles had eroded their way through the walls and projected on the peritoneal surface of the uterus. In 1889 Sanger removed a uterus on account of malignant disease: when the organ was cut across the surfaces thus exposed presented patches of soft tissue, resembling in colour the contents of a ripe pomegranate. This tissue, when examined microscopically, led Sanger to believe that it was derived from the decidua. In consequence, he described the

growth as deciduoma malignum, believing the disease to be a malignant tumour arising in the decidua. This observation was the starting-point of all we know with regard to this dreadful disease of the uterus, which later observers have shown not to be due to the decidua, but to the cells which crown the villi taking on malignant changes and behaving like can-



FIG. 10.—Microscopic appearance of a chorionic villus from a hydatid mole, in transverse section.

cerous epithelium. It is now called chorion-epithelioma. There are two types of cells met with in this disease. In one the cells resemble the large multinuclear mass which caps the villus, and which is known as the syncytium, and the other, which is developed from Langan's cells, produces a much smaller type of cell. But you need not go into these distinctions so long as you remember that the disease known as chorion-epithelioma is a form of malignant disease due to malignant change taking place in the

epithelium of the villi; in the syncytium and in the cells of Langhan's layer.

Here is an admirable diagram showing very well the changes in connection with the villi. It is a drawing from one of Teacher's admirable specimens (Fig. 11). You see a villous tuft and a large collection of decidual cells with big nuclei, decidual cells with many nuclei,

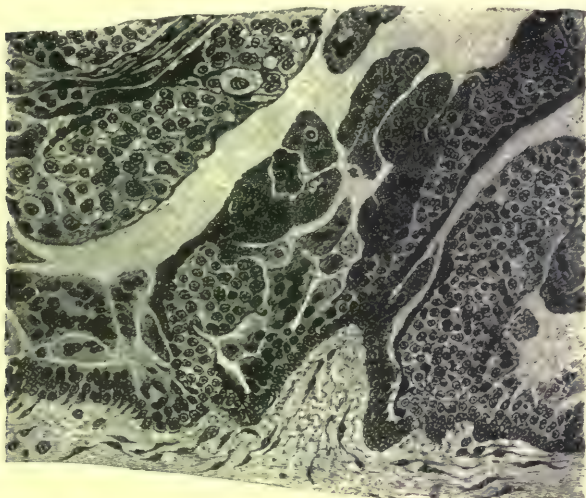


FIG. 11.—Portion of a chorionic villus from a chorion-epithelioma, showing the origin of the tumour from the epithelium of the villi. (After John H. Teacher.)

and syncytia crowding each other in the section. There is another remarkable thing, in which this growth differs from every other form of malignant disease that we know. In every other kind the cells are collected together in alveoli or spaces formed by strands of connective tissue, which we speak of as the stroma. A chorion-epithelioma possesses no stroma. It consists entirely of the peculiar cells which in their usual features are identical with the epithelium, which covers the chorionic villi. These tumours are remark-

able in respect of the symptoms to which they give rise. They occur in the uterus after a miscarriage or a labour connected with hydatidiform disease of the villi, and set up irregular hæmorrhages. The cells are so aggressive that they make their way through the walls of a vein, and bud into its lumen, and pieces are detached and transported to various parts of the body, especially the lungs; and as I told you in the first lecture, the blood attempts to deal with these things by setting up thrombosis and destroying them. But as long as the supply continues you get the disease distributed, and if the uterus is allowed to remain in the body the patient rapidly dies. When the disease is recognised early and the uterus removed, the supply of malignant cells ceases, and the blood is capable of dealing with those scattered cells, and the patient may survive. Taking it altogether, chorion-epithelioma is a very remarkable disease; it is interesting as being a form of malignant disease which has been absolutely detected by the microscope, aided by staining methods, and it has been differentiated from that lumber-room of tumours known as malignant disease. Chorion-epithelioma is common in Germany, and fairly common in America, but it does not seem to be quite so common in this country. It is true that a fair number of cases have been detected in England, and reported to the obstetrical societies and in various papers, but, considering the large number of cases which have been published in Germany, and remembering at the same time that in this country a large number of young obstetric physicians and gynæcologists are on the look-out for cases, the number reported in this country is very small.

It is therefore important for you to remember that if a woman, believed to be pregnant, discharges grape-like bodies from the genital passage, she should be kept very carefully under observation, and, if she should by

any chance complain of irregular uterine hæmorrhages, and particularly if she develops lung symptoms and spits up blood, it is your duty to investigate her condition, and keep in mind the probability that she may be suffering from this remarkable malignant disease arising from perversions of the epithelium covering the chorionic villi. There is one other point I want to draw your attention to, and it is this: in all that I said to you about cancer, up to this point I have been trying to impress upon you the enormous vitality possessed by the epithelial cell; it seems almost indestructible, grows on its own account, and possesses the power to do all sorts of extraordinary things. There must be something which stimulates the cell to do this; there must be a parasite somewhere. Take the sex cell. Two ovaries of a healthy young woman contain some 70,000 eggs. Fortunately for the world they do not all come to maturity, but there those cells lie, and they may be shed week by week or month by month, and unless spermatozoa happens to meet them they are wasted. But if a spermatozoon gets access to an ovum the stimulus it receives from it will lead to the production of another individual. And in all these wonderful changes, apart from the production of an individual, this malignant disease may be started by the contact of one spermatozoon with that remarkable epithelial cell, the ovum. It took many centuries for man to find out what it is that stimulates the ovum to form a new individual; as a matter of fact the real part played by the spermatozoon in fertilising the ovum has only been known about sixty years; need we therefore complain that it has taken much labour to find the cause of cancer? It must be a parasite, something which stimulates the normal epithelial cells of adult individuals to rapidly multiply in the same way that the male gamete, or spermatozoon, initiates reproductive changes in the female gamete, or ovum.

CANCER OF THE GALL-BLADDER.

VII.

It may seem waste of time to devote a whole lecture to the consideration of cancer of the gall-bladder, especially as the current text-books of surgery dismiss the matter in a short paragraph. It may also surprise you to learn that many works on general surgery written ten years ago contain no reference to this subject. Twenty years ago very little information concerning cancer of the gall-bladder was obtainable, and it remained more or less a pathological curiosity until the aggressiveness, enterprise and resourcefulness of modern surgeons have shown that it is a frequent disease, and is of clinical importance. Moreover, the frequency with which cancer of the gall-bladder and gall-stones co-exist has invested the association with a great pathological and practical interest in connection with the cancer problem. In this lecture I intend to discuss the subject from the clinical standpoint, especially in its bearing on the influence of environment in enhancing the deadly consequences of cancer. I shall also consider the epithelial changes in their bearing on the cause of cancer generally.

At the outset it will be necessary to briefly review the epithelial arrangements connected with the drainage system of the liver.

Physiology teaches us that bile, like urine, is purely

excrementitious, and the liver, in addition to its glycogenic functions, may be regarded as a great organic filter, which separates not only toxins from the blood conveyed to it by the portal vein, but also micro-organisms which enter the portal circulation from the gastro-intestinal tract. The method by which the excrementitious bile is conveyed from the recesses of the liver to its outfall in the duodenum involves a brief consideration of the canal system of this organ. The bile-passages arise in the most intimate association

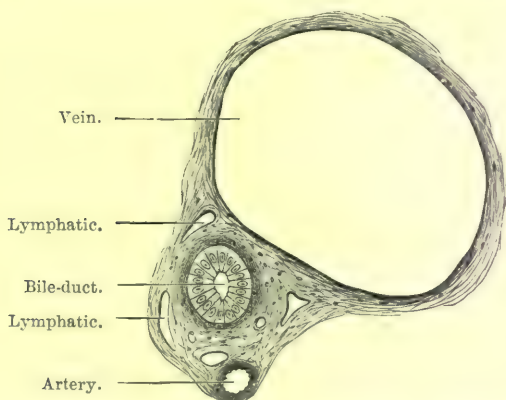


FIG. 12.—Transverse section of a portal canal, showing particularly the bile-duct with its epithelium. (After Schäfer.)

with the hepatic cells; there is reason to believe that they begin as minute canals in the protoplasm of these cells, but it is certain that they become obvious to the microscope as minute intercellular passages, or bile canaliculi, which communicate with the bile-ducts ramifying in the interlobular connective tissue. The bile-ducts around the lobules possess connective-tissue walls and are lined with short columnar epithelium, but in the portal canals the ducts are larger and the epithelium is columnar. The bile-ducts converge to the portal fissure, and, enlarging as they become

confluent, issue as the right and left hepatic duct respectively. These conjoin to form the hepatic duct, which, as it issues from the transverse fissure of the liver, receives the cystic duct descending from the gall-bladder; together they form the common bile-duct, which opens into the second part of the duodenum.

From this account it will be seen that there is a continuity of epithelium from the duodenum to the inmost recesses of the liver, but it is customary and convenient to speak of the canals and canaliculi within the liver as intra-hepatic, whilst the larger ducts, from the points where the hepatic ducts emerge into the portal fissure to the termination of the common bile-duct in the duodenum, are usually termed the "excretory apparatus of the liver"; this consists of the hepatic duct, the cystic duct, the gall-bladder, the common bile-duct, and the ampulla (the diverticulum of Vater).

The epithelial perversion commonly known as cancer may arise in any part of this drainage system of the liver, but it is more frequent in the excretory apparatus than in the intra-hepatic canals.

Cancer arising in the portal canals or in the bile canaliculi is probably uncommon, and when present it is rarely amenable to surgery, indeed, it cannot be distinguished from carcinoma arising from the true hepatic cells until after death. It is of interest to the pathological histologist because, as Rindfleisch pointed out, a primary cancer arising in the intra-hepatic canals exhibits a tubular arrangement, and I well remember examining many years ago some sections prepared from cancerous nodules in the lungs, secondary to a primary carcinoma of the liver, which showed a series of tubules in section lined with columnar epithelium and possessing all the histological features of a bile-canal surrounded by normal pulmonary tissue.

It is not my intention to deal with intra-hepatic cancer, but to confine our attention to this disease as it occurs in the excretory apparatus, and as it is more common in the gall-bladder than in the main duct let us consider its leading features as we can study them in this receptacle.

CANCER OF THE GALL-BLADDER.

This disease has attracted great attention in recent years ; this is in a measure due to its frequent association with gall-stones and also on account of its excessive malignancy. Cancer arises in any part of the gall-bladder ; the course of the disease and the clinical signs which accompany it are modified by the situation of the primary growth. The presence of gall-stones in cancerous gall-bladders is probably as frequent as 95 per cent. ; let me in this part of my lecture merely mention the fact that many surgeons regard the existence of gall-stones in the gall-bladder as a pre-cancerous condition. I will offer you some criticisms on this matter in the next lecture.

In whatever part of the gall-bladder this disease arises it will tend to infiltrate the walls and fill its cavity with cancerous tissue ; consequently when the disease has run its course it will be difficult, and, indeed, often impossible to decide the particular spot in which it started.

There is a specimen in the museum obtained after death from an old man : the gall-bladder is replaced by a mass of cancer containing a number of polygonal-shaped gall-stones nested in its centre, and were it not for this nest of concretions we should have been unable to detect the gall-bladder, so thoroughly have its tissues been destroyed. In another obtained from a woman, aged fifty-six years, the gall-bladder is as big as a cocoanut ; the cancer is represented by a pultaceous mass

which gave rise to a sense of fluctuation on palpation during life ; so distinct was this that it gave me the impression that the trouble was due to a calculous cholecystitis and that the gall-bladder contained fluid. This induced me to expose and open the gall-bladder. I found eighty-six almost pure cholesterol calculi resembling polygonal lumps of spermaceti embedded in the soft growth.

In another class of case the gall-bladder will not be much enlarged ; its walls, however, will be thickened, very hard, and so tightly contracted on the gall-stones within it that they will be as firmly packed as a tessellated pavement, and efforts to extract them will almost invariably cause the concretions to break up rather than separate from each other.

Occasionally the cancerous process will start in a calculous gall-bladder, and without altering the contour of this receptacle will quickly infiltrate or permeate the adjacent tissue of the liver, and in a few months the dividing line between the gall-bladder and the hepatic tissue will be completely obliterated (Fig. 13).

The number of concretions in a cancerous gall-bladder varies enormously. The museum of Charing Cross Hospital contains a gall-bladder showing a primary cancer arising at its neck and extending into the cystic duct. A solitary gall-stone is embedded in the cancerous mass.

The only example of a cancerous gall-bladder unassociated with gall-stones which has come under my observation happened to be the first I saw in a living subject. In this instance the disease arose at the fundus of the gall-bladder of a man and formed a patch of new growth, in superficial extent as large as a thumb-nail, but it infiltrated and penetrated the wall ; a small bud-like process of growth, not larger than a currant, projected on the serous surface of the gall-bladder and infected the peritoneum. Every structure in the belly

was beset with minute cancerous nodules. The abdomen was inconveniently distended with fluid. The physician in charge of the patient could not account for the hydroperitoneum, and at his request an operation was



FIG. 13.—A cancerous and calculous gall-bladder in section, showing the manner in which the liver is infiltrated. (Museum of St. Bartholomew's Hospital.)

undertaken. The evacuation of many pints of fluid afforded temporary relief and established the diagnosis.

One of the most remarkable examples of this disease which has come under my notice occurred in an aged spinster, who knew for several years that she had a large abdominal tumour which was regarded as a sub-

serous uterine fibroid with a long and slender pedicle. In course of time her health deteriorated, and free fluid (hydroperitoneum) collected in the belly. It was decided to evacuate the fluid and remove the tumour if possible.

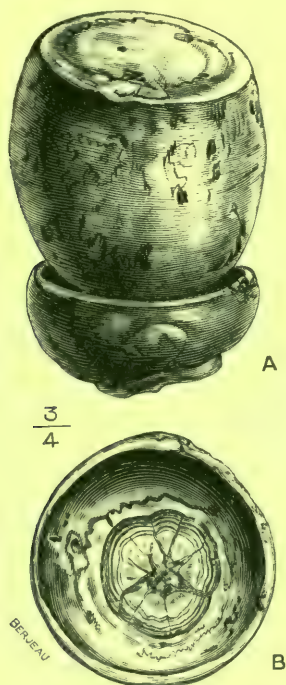


FIG. 14.—A. Two gall-stones adjusted in the form of a mill. B. The nether gall-stone with its polished surface exposed. (From a cancerous gall-bladder.)

At the operation this tumour, which reached to the hypogastrium, proved to be a huge gall-bladder. I succeeded in removing it, and was disappointed to find numerous secondary nodules in the right lobe of the liver. After a thorough examination of the internal organs I failed to discover a primary cancer. After completing the operation an examination of the gall-

bladder disclosed an extraordinary condition. A calculus firmly impacted in the cystic duct had led to the production of the condition known as *hydrops vesicæ felleæ*, the largest example that has ever come under my notice. The large cavity contained two remarkable gall-stones, for one of them resembled an acorn and the other its cup (Fig. 14). The concavity of this shallow cup was occupied by the rounded pole of the balanoid calculus, and the two bodies had freely moved on each other, for their opposed surfaces are polished as the result of the trituration. The relation of these two gall-stones vividly recalled to my mind the glacier-mills, which form such interesting objects in the famous glacier garden of Lucerne.

So far as the patient was concerned the most sinister object in this huge gall-bladder was a patch of cancerous material infiltrating its walls and which was the source of the material causing the secondary nodules so conspicuous in the liver.

Gall-stones are often numerous when associated with cancer. The gall-bladder represented in Fig. 15 is interesting in this respect, for it contained several hundred almost pure cholesterin calculi. The specimen is remarkable; I removed it from a woman, aged forty-three years, in whom it caused no pain; the patient was merely inconvenienced by the presence of a lump which she could feel in the abdomen. On examination it had the characteristic contour of an enlarged gall-bladder, but the unusual hardness of the mass made me regard it as cancerous. When the organ was exposed in the course of the operation it had contracted an extensive adhesion to the adjacent omentum and transverse colon, for the growth, which filled the gall-bladder, had burst through the wall near the fundus, and, fungating freely, had infiltrated the wall of the colon. The neck of the gall-bladder was fairly free from the cancer and the liver had escaped infiltration, but the implication of the

transverse colon proved a serious matter, and in order to remove the disease I found it necessary not only to



FIG. 15.—An enlarged (cancerous) gall-bladder removed from a woman, aged forty-three years. The cancer had burst through the fundus of the gall-bladder and implicated the transverse colon. Eight inches of the latter was resected. Several hundred calculi, consisting almost entirely of cholesterin, were present.

extirpate the gall-bladder but to resect eight inches of the colon and a large area of omentum. The cut ends

of the gut were easily joined by suture, and the patient made a rapid recovery from the operation to die fourteen weeks later from recurrence.

The tumour on microscopic examination proved to be a perithelioma (endothelioma). This is a matter of pathological interest, because in most of the gall-bladder cancers which have come under my notice the subcolumnar and spheroidal type of cells prevailed.

In regard to the type of cells prevailing in cancerous gall-bladders, it may be mentioned that in an example which I removed from an elderly spinster the infiltrated walls of the gall-bladder were tightly contracted on the concretions. When the cancerous mass was examined in the laboratory it was found to be composed of typical squamous cells and abounded in cell-nests. This is an example of mutation of epithelium due to pressure, such as occurs in the intestinal mucous membrane exposed in a colotomy opening, or in the uterine mucous membrane covering a polypus extruded from the uterus into the vagina, and under other conditions.

The implication of the colon, which was such a prominent feature in this case, is a matter of importance in regard to diagnosis. Throughout this course of lectures it has been my endeavour to impress upon you the insidious way in which cancer arises in the viscera and makes steady progress without producing symptoms, until it so interferes with the function of the affected, or of the adjacent organs, that the life of the individual is in grave peril. This is illustrated in a striking way by the clinical signs present in a woman with a cancerous gall-bladder recently in my ward. She was sent in with a diagnosis of calculous cholecystitis. On admission I regarded an obvious tumour in the right hypochondrium as a cancerous lump in the tranverse colon, as it lay well below the line of the costal cartilages. At the operation it proved to be a

cancerous and calculous gall-bladder; the disease involved the fundus of the gall-bladder and was firmly adherent to the adjacent colon. Though the patient was a spinster, aged seventy-three years, I succeeded without difficulty in extirpating the gall-bladder, and the cancerous nature of the growth was substantiated in the laboratory.

Cancer of the gall-bladder is more common in women than in men, and it is a disease of advanced life; probably the period of greatest liability is the interval between the fiftieth and sixtieth years. It is most insidious in its beginning, notwithstanding the presence of gall-stones. The patients usually seek advice either on account of a local lump which they have detected or for a marked depreciation of health. In my experience there are two distinct conditions which present themselves in this disease. In one a more or less movable pyriform swelling exists in the right hypochondrium associated with a slight tinge of jaundice; this swelling resembles in all particulars an enlarged gall-bladder, but the local signs are not so acute as in cholecystitis, yet there is usually such an obvious impairment of the general health as to make one suspect the malignancy of the lump. In the late stages of the disease hydroperitoneum is present.

In the other class the patients come under observation with signs and symptoms indicating serious disease which resemble those peculiar to the gall-bladder, mingled with others pointing to cancer of the liver. In many instances it is impossible to decide from physical signs which organ is diseased until the parts are exposed in the course of an operation. In some instances the disease is proved to be calculous cholecystitis; in others it is a cancerous gall-bladder; in a few primary cancer of the liver, and occasionally a gall-bladder will be found to contain calculi, whilst the liver presents nodules of cancer, secondary to a primary

focus of disease in some part of the gastro-intestinal canal. Occasionally a cancerous lump supposed to be in the gall-bladder is situated in the transverse colon or the pyloric region of the stomach.

Primary cancer of the gall-bladder runs a rapid course, and usually terminates the life of the patient within six months of the onset of definite symptoms. Jaundice is present in the late stages of the disease in about one third of the cases.

Cancerous gall-bladders are sometimes successfully removed by surgeons, but when a large number of hospital cases are analysed the results cannot be considered encouraging. In the year 1905 seventeen patients with primary cancer of the gall-bladder were submitted to operation in the chief general hospitals in London; of these nine died.

Unfortunately by the time a cancerous gall-bladder is discovered the opportunity for a successful operation has usually passed.

I shall discuss the relationship of gall-stones to cancer of the gall-bladder in the next lecture.

ON CANCER OF THE BILE-DUCTS AND DUODENUM.

VIII.

IN the last lecture I reiterated, with perhaps depressing monotony, that primary cancer of the gall-bladder is an insidious disease rarely accompanied with definite signs and symptoms until the disease has passed beyond the bounds of hopeful surgery. In describing cancer of the large extra-hepatic ducts, including the ampulla, I shall have to repeat that when this disease arises in these ducts it begins insidiously and gives rise to few signs, but it differs from cancer of the gall-bladder in one important particular, namely, jaundice; this is the earliest and most persistent sign when cancer attacks the ducts forming the excretory apparatus of the liver. One of the features which will probably attract your attention when you have an opportunity of studying a recent case is the small amount of cancerous material which leads to such disastrous consequences. Fortunately a primary cancer in any portion of the extra-hepatic ducts is rare, but a sufficient number of cases have been recorded to allow a systematic account of the chief clinical features of the disease to be written.

Cancer may arise at the junction of the two hepatic ducts, or at the union of the hepatic and cystic duct, or in any part of the common duct, or in the ampulla itself. Carcinoma arising in the head of the pancreas and in the mucous membrane of the duodenum, near

the bile-papilla, will obstruct the outflow of bile and produce symptoms indistinguishable from those due to cancer arising in the common duct, and of these obstructive jaundice is the most obvious. To the naked eye cancer of the bile-ducts looks like a knob of tough fibrous tissue blocking up the duct; in some cases the duct appears as if embedded in a mass of tough fibrous material, but on microscopic examination this growth is seen to be made up of columnar or spheroidal epithelium, and in some specimens a tubular or gland-like arrangement is obvious, in which case it is sometimes termed an "adeno-carcinoma." In all cases, however, the blockading effects on the ducts are the same, although the precise results produced vary according to the position of the obstruction. These varying effects are carefully studied by surgeons, as they are useful aids in what is known as differential diagnosis. For example, the presence of cancer in the extra-hepatic ducts not only completely hinders the escape of bile into the duodenum but leads to dilation of the canals above the obstruction, including the intra-hepatic canals. This also induces, as a consequence, enlargement of the liver, and in some cases the intra-hepatic canals are so dilated that a section of the liver resembles a sacculated kidney (Fig. 16).

The situation of cancer in the bile-ducts is important in its effects upon the gall-bladder, for when the disease arises at the junction of the two hepatic ducts—a common situation—the supply of bile to this receptacle will be cut off, whereas when the blockade is well below the junction of the cystic and the hepatic duct the gall-bladder will become over-distended with bile, and can often be felt as an oval body lying in the hypochondriac or right lumbar region. It may be mentioned here that the condition of the gall-bladder is a valuable guide in the differential diagnosis of obstructive jaundice. It has been determined by

observation that when escape of bile into the duodenum is completely arrested by cancer in the common bile-



FIG. 16.—Liver in section, showing dilatation of the intra-hepatic bile-canals secondary to primary cancer of the common duct.

duct, or the ampulla, or when cancer arising in the head of the pancreas implicates the common duct, the

bile-ducts and the gall-bladder become distended and dilated in response to the pressure of the bile accumulated within them. In these circumstances the gall-bladder will become so big that it may be felt as a large, pear-shaped lump lying in the right lumbar region. When the cystic duct is obstructed the gall-bladder passively enlarges from the accumulation of the mucus secreted by its own glands. On the other hand, when the common duct is occupied by calculi the gall-bladder is smaller than usual, and is, as a rule, tightly contracted on any biliary concretions it may contain. For detecting these contrasted conditions we are indebted to Courvoisier. This rule is sufficiently constant to be useful in practice, but there are exceptions, and it may be useful to describe one.

For instance, it was pointed out in dealing with cancer of the gall-bladder that this disease may arise in the mucous membrane in any part of this receptacle. Thus in the specimen represented in Fig. 17 the cancer arose in the neck of the gall-bladder and extended into the cystic duct and formed a sort of collar around a solitary gall-stone. Even such an extensive mass of cancer in the neck of the gall-bladder would not cause jaundice. It is, however, easy to realise that if the cancer extended along the cystic into the hepatic duct there would be obstruction to the escape of bile from the hepatic duct, which would lead to jaundice. Such a case has been observed and carefully recorded.

The great interest of these cases centres around the diagnosis. When a patient suffers from persistent, profound and unvarying jaundice, it at once becomes an important question for the patient's welfare to determine the nature of the obstruction. If the blockade is due to a gall-stone in the common duct, or, in the case of persistent and profound jaundice accompanied by emaciation, to the consequences of a

calculus in the ampulla, which not only blockades the bile-duct, but also the pancreatic duct, it is an important matter to remove the obstructing stone. An operation in these circumstances will in all probability prolong the patient's life. On the other hand, if the obstruction be due to cancer the patient will not be benefited and perhaps his life will be materially shortened.

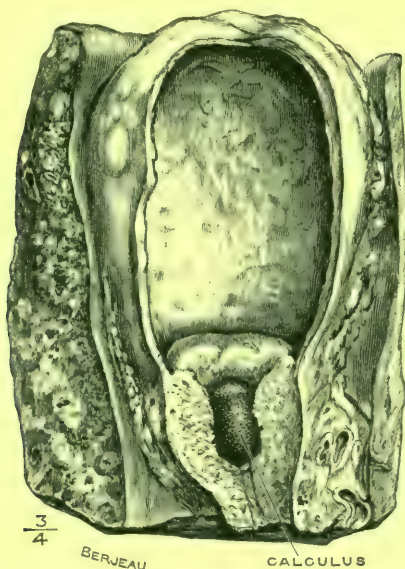


FIG. 17.—A gall-bladder with a primary cancer arising in its neck and extending into the cystic duct. The gall-bladder was filled with pus. The patient, a man, aged seventy years, died nine months after the beginning of his symptoms. (Museum of Charing Cross Hospital.)

Until you become more thoroughly acquainted with the difficulties of diagnosis, you will often be astonished to watch a surgeon open the abdomen of a patient deeply jaundiced hoping to find a calculus in the common duct, or in the ampulla, and on examining the duodenum with his fingers he finds a hard body occupy-

ing the position of the bile-papilla, yet he cannot satisfy himself of its nature. He then makes an incision into the wall of the second portion of the duodenum and exposes the papilla, still hoping to find a stone in the ampulla, but to his chagrin finds a small knob of cancer. In such a case Halsted found a carcinoma of the ampulla, which he promptly excised with the bile-papilla and the adjacent section of the common duct; the cut end of the duct he implanted into the duodenum. The patient recovered from the operation, but died several months later from recurrence. Similar cases have been recorded. The operation of removing a gall-stone from the ampulla by means of an incision through the duodenum is known by the portentous term "trans-duodenal choledochotomy." It is an interesting and satisfactory procedure, and if you carefully watch the parts as the surgeon gently squeezes the stone through the opening after incising its edge, the escape of the calculus is followed by a jet of fluid. This is usually bile, but sometimes it is clear fluid; in the latter case this is of serious import, as I will endeavour to explain.

When the escape of bile into the duodenum is completely cut off the liver continues to excrete bile, and the pressure in the bile-ducts will continue to rise until resorption takes place and the bile finds its way into the blood, causing that yellowness of the tissues which we call jaundice. The bile under such pressure finds its way into the interlobular lymphatics, and is carried into the thoracic duct and thence enters the blood-stream. When this mingling of blood and bile (cholæmia) has existed for several weeks the coagulation-rate of the blood is lowered, and it is an established fact that operations on patients who have been deeply jaundiced for several weeks are liable to be complicated with an uncontrollable oozing of blood, and the patient bleeds to death in the same manner as

after splenectomy performed for a leukæmic spleen. I learned this fact very early in my surgical career. I read books devoted to diseases of the liver for the purpose of ascertaining particularly in cases where the escape of bile is prevented by cancer of the duodenum invading the papilla ("circum-ampullary cancer" as it is sometimes called), or when it arises in the head of the pancreas, whether the lethal effects of the cancer were in any way hastened by the consequent jaundice. No information was forthcoming. This induced me to try the effect of conducting the bile into the intestine by anastomosing the gall-bladder and the transverse colon.

My first observation was made on a woman jaundiced in consequence of carcinoma of the head of the pancreas. In this instance the skin was of that deep green hue which is sometimes called "malignant" or "black jaundice." The gall-bladder, which could easily be felt as a large ovoid body lying below the ribs, was exposed through an incision in the line of the right rectus muscle, and through a small opening made at its fundus the bile was allowed to run away; the edges of the opening were then sutured to the edges of a hole made in the wall of the transverse colon immediately adjacent. The wound in the abdominal wall was carefully closed with sutures. During the two days following the operation an enormous quantity of bile escaped by the anus—indeed, the patient suffered for forty-eight hours from a profuse biliary diarrhœa. During this period the wound oozed blood freely, and nothing would check it. She died a few days after the operation, and we found that a similar oozing of blood had taken place around the edges of the wounds made in the colon and gall-bladder for anastomotic purposes, and in the tracks of the sutures; and no union had occurred between the gall-bladder and the colon. Since that date I have been successful in several cases

in effecting a junction between the gall-bladder and colon in patients with obstructive jaundice due to cancer by performing the operation at an earlier stage, that is, before the jaundice became too intense. As a result of these operations I have satisfied myself that jaundice does not hasten the fatal event, except in so far as it directly imperils the patient's life from hæmorrhage when operative measures are undertaken. It is well, therefore, that you should be informed on this point, that in severe and progressive cases of jaundice where there is difficulty in deciding whether the obstruction depends on a calculus impacted in the ampulla or a cancer in that situation; the matter can only be determined in the course of an operation, therefore surgical interference should not be deferred until the jaundice is of such intensity that an operation is attended with grave risks from hæmorrhage, nor should you be induced to embark on such an undertaking in the belief that by giving the patient chloride of calcium you may be able to increase the coagulability of the blood. Let me also remark that if you explore the bile-ducts and find the escape of bile obstructed by cancer, either of the common duct, the ampulla, the duodenum, or the head of the pancreas, you will make your patient comfortable and certainly earn his gratitude by anastomosing the gall-bladder with the duodenum, or jejunum if you can, or with the colon, as this will relieve the jaundice and the intense itching (pruritis) of the skin which is such an intolerable nuisance to icteric patients. This operation is denoted by the sesquipedalian term, "cholecyst-enterostomy."

There are one or two facts connected with obstructive jaundice due to diseases of the head of the pancreas which are worth attention. When cancer arises in the head of this gland it causes jaundice by obstructing the terminal segment of the common bile-duct, which either traverses a canal in the gland or lies in direct

contact with it. The actual obstruction may be due to pressure on the duct, or this structure is sometimes actually implicated by the malignant growth.

The method of determining whether the jaundice is due to cancer in the head of the pancreas in the course of an operation may be described as "rough and ready," for it consists in simply feeling it with the fingers. As the gland may be enlarged and hard from chronic pancreatitis as well as from cancer, the fingers are unable to distinguish between the two conditions. It has happened that in cases where cholecyst-enterostomy has been performed as a palliative measure under the impression that the patient's trouble was due to cancer, he has recovered, the tumefaction of the pancreas being really due to pancreatitis.

There is, however, a peculiar tint about the jaundice associated with cancer of the head of the pancreas which greatly assists diagnosis. The jaundice, which is usually unaccompanied by pain in the early stages of this disease, lacks the saffron yellowness which is seen when the common bile-duct alone is obstructed, and assumes a somewhat mahogany tint, which is very characteristic, and in those patients in whom the bile has been successfully diverted into the alimentary canal the yellow element in the coloration of the skin, and the itching disappear, but the peculiar brown tint, which resembles the bronzing of Addison's disease, persists. No satisfactory explanation of the brown hue of the skin is forthcoming. It is, however, a valuable aid in diagnosis.

It has already been mentioned that when the flow of bile along the common duct is completely stopped by an obstruction of any kind, the bile is drained away by the lymphatics into the circulation and its final escape is effected by the kidneys. In the early days of the obstruction, if the common bile-duct be exposed and incised in the course of an operation it will be

found distended with bile. When the blockade of the duct has been maintained many weeks (six or more) it happens now and then that the duct no longer contains bile, but a colourless fluid, probably mucus. This is a sinister sign, for surgeons who have had a wide experience of what is conveniently called "gall-stone surgery" state that in these circumstances the patients almost invariably die shortly after operation. My observations agree with this.

It should also be mentioned that in some cases of cancerous obstruction of the common duct the gall-bladder becomes so distended with bile, or bile mixed with pus, that the wall ulcerates, and then a perforation occurs and the patient dies from acute peritonitis due to the escape of septic material which it contained. Careful records of such disasters are available. I have known a case of primary cancer of the gall-bladder to terminate in this way.

Cancer in the excretory ducts, like this disease in the gall-bladder, is most common between the fiftieth and sixtieth years. It is also useful to bear in mind that cancer in any situation in the excretory apparatus of the liver is not usually accompanied by pain. It however, must always be remembered that a gall-stone may painlessly obstruct the common duct, producing profound jaundice; on the other hand, cancer will sometimes obstruct the duct and set up attacks of pain resembling biliary colic.

The great point in which cancer of the common bile-duct, or its ampulla, differs from cancer of the gall-bladder is this:

Cancer in the gall-bladder nearly always co-exists with gall-stones, whereas the presence of gall-stones in association with cancer of the common bile-duct is exceptional.

CANCER OF THE DUODENUM IN RELATION TO OBSTRUCTIVE
JAUNDICE.

Primary carcinoma in any part of the small intestine is uncommon, but it occurs more frequently in the duodenum, short as it is, than in the jejunum or ileum. It is also remarkable that the pylorus should be so frequently attacked by cancer—indeed, it is one of the three commonest situations in which this disease arises—while the succeeding twelve inches of the alimentary canal is almost immune, yet it is often the seat of ulceration. There can be little doubt that a cancerous ulcer of the duodenum would often escape detection were it not for the fact that the disease is apt to arise in the immediate vicinity of, and often involves, the bile - papilla, leading to obstructive jaundice. The circum-ampullary carcinoma of the duodenum leads to distension of the bile-ducts and the gall-bladder, but the course of the disease differs somewhat from that seen in cases where the disease arises in the ampulla or in the common duct, because the cancerous ulcer on the surface of the duodenum is liable to become infected and then it sloughs; the infection will extend into the bile-ducts and set up suppurative cholangitis with its usual accompaniments, fever and rigors, ending in death from sepsis.

I may take this opportunity of relating the facts of a somewhat unusual case of cancer of the duodenum which has some bearing on this subject. A man, aged fifty-six years, was invalided from Burma on account of persistent vomiting and rapid emaciation. A malignant growth somewhere in the gastro-intestinal tract was suspected but no lump could be felt anywhere. The vomiting resembled that seen in the condition known as "vicious circle," which occasionally happens after the operative procedure known as gastro-jejunosotomy. I decided to set the diagnosis at rest by

examining the alimentary canal through an abdominal incision. The stomach, the small and the large intestines were examined carefully and nothing appeared to explain the symptoms, but on turning the stomach upwards to examine its posterior surface I saw a small contracting growth in the middle of the third part of the duodenum. This hard ring of growth had completely obstructed the lumen of the duodenum so that the bile and pancreatic juice regurgitated into the stomach, where they mingled with the gastric juice and ingested fluids, to be ejected in the form of filthy vomit.

The duodenum above the stricture was enormously dilated and produced an appearance not unlike a double stomach. The growth had involved the duodenum and was so closely adherent to the superior mesenteric vein that its removal could not be entertained. I performed posterior gastro-jejunostomy and then anastomosed the greatly distended duodenum with the limb of the jejunum descending from the new stoma, so as to drain the bile and pancreatic fluids direct into the small intestine.

The immediate results of the operation were admirable. The vomiting ceased and the patient began to take and assimilate food; his pain ceased and we entertained hopes that his life might be prolonged. About thirteen days after the operation he had severe cardiac dyspnoea, then circulatory troubles supervened, from which he died. However, the last fourteen days of his life were made comfortable by the operation.

THE RELATIONSHIP OF GALL-STONES TO CANCER OF THE GALL-BLADDER.

It has been already mentioned that the frequent association of gall-stones and cancer of the gall-bladder has led some surgeons to regard a calculous cholecystitis

as a pre-cancerous condition. Let us review the facts and satisfy ourselves as to how far they support this view. Careful observations and investigations into the conditions underlying the formation of gall-stones, especially by Naunyn, have shed much valuable light on this matter. Gall-stones are mainly composed of cholesterin, and this material is collected around a nucleus which may consist of shed epithelium and clumps of bacilli; the cholesterin is mixed in varying proportions with a cementing substance known as bilirubin-calcium. Cholesterin was formerly regarded as a deposit from the bile, but it is now known that this singular stuff is furnished by the epithelium lining the gall-bladder and the larger ducts, especially when inflamed. Occasionally the crystals of cholesterin can be seen on the mucous membrane of an inflamed gall-bladder, sparkling like the tinsel on the coat of a harlequin. Many observations have been published in which an attack of typhoid fever preceded the cholelithiasis, and the *Bacillus typhosus* has been found in the gall-bladder twenty years or more after patients have recovered from the fever. Moreover the relationship between micro-organisms, cholecystitis, and gall-stones has been established by the experimental production of gall-stones after injecting attenuated cultures of micro-organisms into the gall-bladders of dogs. It is now regarded as proved that the favouring conditions for the formation of gall-stones are catarrh of the epithelium lining the gall-bladder and the bile-ducts, and the presence of micro-organisms, especially *B. typhosus*.

A valuable demonstration of the origin of cholesterin from the epithelium of the gall-bladder is afforded by those cases in which the cystic duct is so completely plugged by a calculus that bile no longer finds its way into the gall-bladder. In these circumstances the gall-stones which form subsequent to the obstruction of the cystic duct consist of pure chole-

sterin and look like polygonal lumps of spermaceti. The same conditions exist in cases where the cystic duct is plugged by cancer.

One of the first conclusions which is forced on the mind of the surgeon when he reflects upon the condition of organs antecedent to the occurrence of cancer is that this dread disease is more liable to attack an organ which has been the seat of previous disease than one which is obviously healthy. The opinion which I hold very strongly is this: The pathological conditions of the epithelium lining the gall-bladder which cause it to produce cholesterin in abundance increase its vulnerability to the micro-parasite of carcinoma. It is illogical to urge that cancer of the gall-bladder is due to gall-stones when this disease occasionally arises in a gall-bladder which has never been occupied by calculi; moreover, when cancer arises in the large excretory ducts of the liver it is exceptional to find the disease associated with gall-stones.

The fact that patients with chronic calculous cholecystitis are more liable to carcinoma of the gall-bladder than an individual with a healthy bile-receptacle is used, and rightly, as an argument that such calculi should be removed by operation. I go a step further and urge that such unhealthy gall-bladders should be removed. This recommendation has been questioned on the ground that there are very few instances known in which patients who have had biliary concretions removed from their gall-bladder (cholecystotomy) have again come under observation with cancer of the gall-bladder. This side of the question has not been investigated with any zeal. I have satisfied myself by following up the after-history of patients who have had cholecystotomy performed and have passed out of the hands of the surgeon with a biliary fistula, that some of them have died from cancer of the gall-bladder. In one instance known to me the

patient had a biliary fistula five years before cancer supervened. If more attention is given to this matter, and its importance be realised by those who have the care of patients with persistent biliary fistulæ, some valuable evidence would soon be available. The more I study this aspect of the "gall-stone question," the more convincing the evidence appears, that when an operation becomes necessary for calculous cholecystitis the surgeon acts in the best interests of his patient when he removes the diseased gall-bladder.

Since this lecture was delivered a valuable observation has been published by Mr. H. Lett, in which primary cancer of the gall-bladder was detected twenty-one months after cholecystotomy ('Lancet,' 1909, vol. i, p. 1099).

Since I have had every gall-bladder which has been removed in the course of an operation carefully examined microscopically as a routine, I have been astonished at the frequency with which it is the seat of cancer.

ON A COMPARISON OF CANCER OF THE LIPS AND OF THE LABIA.

IX.

THROUGHOUT this course of lectures I have taken every opportunity to emphasise the fact that cancer is more liable to attack an organ which is the seat of chronic disease than one which is apparently healthy. This also applies to the situations in which cancer arises on cutaneous and mucous surfaces, and accounts for the occurrence of carcinoma at the edges of chronic ulcers, whether on the skin of the leg or on the mucous membrane of the stomach, the margin of ulcers due to burns and scalds, X-ray burns, lupus patches and the like. Cases have been reported in which squamous-celled cancer has arisen in the scars left on the conjunctiva as the result of lime burns.

In this lecture I shall endeavour to show that primary cancer of the lips and of the labia support this contention in no uncertain way.

Cancer of the lip is a common disease; you will frequently see examples of it in the out-patient room and in the wards. In these departments you will see this disease in the early and operable stages, but in the inoperable and advanced conditions you will also have opportunities of studying it in the cancer asylum connected with this hospital. I shall assume for the purposes of this lecture that you are familiar with the clinical features of cancer of the lips and of the labia. In its age-incidence it shows nothing uncommon in

comparison with cancer in other regions of the body. Mr. C. W. Rowntree, in a careful statistical study of cancer of the lips contained in the 'Archives of the Middlesex Hospital,' 1906, vol. vii, p. 118, calculated the age-incidence as ascertained from 202 patients to be 56·4 years. He points out that the youngest age at which this disease has been reported, and on the strength of a microscopical examination, is the thirteenth year (Johnstone and Batashoff). A case has been reported in a man of the great age of 103; this patient was submitted to operation by Jalland in 1891.

This disease in the lips does not differ from cancer in other regions of the body in the relentless way in which it destroys the tissues according to the lip affected, and the manner in which it infects the lymph-glands in the submaxillary triangles and the submental space: the gradual fusion of the cancerous lymph-glands followed by the implication and ulceration of the overlying skin, and the formation of a huge cancerous ulcer in the neck, on the floor of which the carotid vessels may be seen pulsating; and in due course the ulceration may breach their walls and lead to fatal hæmorrhage, unless the patient dies earlier from exhaustion produced by repeated small losses of blood, or septic infection of the lungs, due to the inhalation of foul material incident to the septic infection and sloughing of the cancerous tissues.

Cancer of the lip has a great interest for those who are investigating the cause of cancerous diseases, on account of the greater frequency with which it arises in the lips in men as compared with women, and the greater liability of the lower as compared with the upper lip.

In this hospital during the years 1897–1907 (both inclusive) there were fifty cases of carcinoma of the lips admitted into the surgical wards, the greatest number admitted during one year being seven and the least one. Of these fifty patients all were men. In two

men the site of the growth was the upper lip; in the remainder the lower lip was affected, but in three of these forty-eight patients the cancerous ulcer began at the angle of the mouth.

This preference of cancer for the lower lip is shown in a striking way by the cases tabulated by Loos in Brun's Klinik at Tübingen. Out of a total of 565 patients 534 arose in the lower lip, and of these 467 were men and 67 women. It is also remarkable that though men are infinitely more liable to cancer of the lower lip than women, yet the liability is equal for both sexes in regard to the upper lip. In the 565 cases collected by Loos 31 occurred in the upper lip, and of these 16 were men and 15 women. In regard to the lower lip it may be stated that the disease rarely begins in the middle line, and the liability of the right and left halves is practically the same.

The figures given above indicate that men are much more liable to suffer from cancer in the lower lip than women; and that cancer of the upper lip is an uncommon disease, and that the cases are fairly equally distributed between men and women.

The increased liability of men to cancer of the lip as compared with women is attributed to the greater frequency of tobacco smoking among men as compared with women. In connection with this matter it may be mentioned that cancer of the lip is sometimes spoken of as "countryman's cancer," on account of the frequency with which it occurs among agricultural labourers who use short-stemmed dirty pipes. The clay pipes with short stems are very convenient as they can be carried in the pocket. In this hospital some of the patients come under the heading "farm-labourers," but many are men who come under the term "labourers," and their custom in regard to the short pipe is the same as the farm-hand. The stem of such a short pipe soon becomes hot when in use and burns or scorches the lip.

Women, too, who work in the fields acquire the habit of smoking short clay pipes, and, as far as my observations go, in Germany more women work in the fields than is the custom in England. This may account for the greater prevalence of cancer in the lip in women as shown in the tables prepared by Loos, than we find from an analysis of the list from our own hospital.

It is possible that chronic syphilitic ulcers of the lips may become cancerous and account for a certain number of cases which occur in non-smokers. This is undeniably true of the tongue. It is also certain that cancer is occasionally seen in the lips of patients who do not smoke tobacco and who are not tainted with syphilis. It is also worth bearing in mind that cancer of the lip is a common disease among those whom we regard as the "working class," but this set of men and women does not by any means monopolise tobacco. Many professional men, including the vicar of the parish, smoke as hard as the labourer, yet it is excessively rare to find a case of cancer either of the upper or lower lip among them.

The preference of cancer for the lower lip is not easily explained. The distribution of malignant ulcerations of the face is an enigma. How rare it is to find squamous-celled carcinoma attacking any part of the cutaneous covering of the face save the lips, and why should rodent ulcer grow in the skin of the eyelids, the margin of the nasal orifices, and on the cheek, yet be unknown on the chin and lips?

Let me now take you to another part of the body, namely, the labia, where the anatomy is similar to that of the lips, and let us study it in relation to trauma and carcinoma.

The labia majora are two large parallel folds of skin extending from the mons veneris to near the anus; they form the boundaries of the rima pudendi.

The cutaneous outer surfaces of the labia are beset

with hairs and sebaceous glands, and the skin is more deeply pigmented in this part than in other regions of the body. The opposed surfaces of the labia are pink, and possess rudimentary hairs and very large sebaceous glands.

The labia minora are two cutaneous folds lying parallel with the greater labia. They are hairless, but rich in large sebaceous glands. Anteriorly they become confluent at the frænum of the clitoris, but posteriorly they are gradually lost on the inner surfaces of the labia majora.

There are some points connected with the age-changes of the labia which need consideration. During infancy the greater labia appear as two parallel cutaneous eminences, and the thin edges of the smaller labia project between them and resemble mucous membrane. At puberty the hair becomes conspicuous on the outer surface of the labia majora, and these cutaneous folds increase in size and usually conceal the labia minora. Their opposed or inner surfaces remain pink, whilst the outer surfaces become pigmented, especially in brunettes. In many women the labia minora remain concealed by the labia majora, but in others they grow unduly and protrude beyond the vulvar cleft and resemble a pair of molluscan palps. They then undergo a curious change, for those parts covered by the greater labia retain their pinkness, and possess as usual very large sebaceous glands, but the palp-like portions become deeply pigmented and lose their sebaceous glands; occasionally delicate hairs, two or more centimetres in length, grow from them. Labia majora elongated in this way are sometimes termed "hypertrophied nymphæ," a condition which reaches its maximum in Hottentot women, whose "apron" is formed of greatly elongated nymphæ (Fig. 18).

After the forty-fifth year the hair on the mons

veneris and labia, like that on the rest of the body, tends to lose its colour, becomes white, and is gradually shed; the greater labia shrink as the fat disappears, which causes the nymphæ to be exposed and the vulvar orifice becomes narrowed. Occasionally this shrinking of the parts is excessive, and the labia, big and little, become markedly atrophied, so that the



FIG. 18.—The Hottentot “apron.” It is formed of greatly elongated labia minora. (After Blanchard and Lesueur.)

inner surfaces of the labia are exposed; they become smooth and shiny, with here and there red patches which are exquisitely tender. Coincident with such extreme changes the vaginal orifice is narrowed, and in some instances will scarcely admit a finger. The hairs on the labia and mons are scanty, coarse, and broken; finally the labia become almost as colourless as skin, and all the folds and creases look as if they had been smoothed out.

In such extreme cases the patients complain of great irritation, excessive pain during sexual intercourse and micturition. For this condition the name "kraurosis" (*κραῦρος*, dry, withered) is applied, and it is very troublesome and inconvenient in married women, but spinsters rarely complain of it.

No particular cause is known to account for this condition, and it is frequently associated with atrophy of the uterus, and is occasionally seen as a sequel to bilateral ovariectomy, oöphorectomy, and hysterectomy.

Kraurosis is a condition of interest to us, for it may be regarded as a pre-cancerous condition, but before considering this matter I wish to draw your attention to another change to which the vulvar epithelium is prone, and which is also a pre-cancerous condition.

It is well known that the mucous membrane of the tongue in middle-aged men, especially of those who smoke and of those who are syphilitic, often presents irregular white patches, a condition known as "leukoplakia." These white patches are due to thickening of the epithelium and small-celled infiltration of the subepithelial layer. Sometimes these patches are so thick that the affected area of the tongue looks as if coated with white paint. This leukoplakic condition of the lingual mucous membrane is of sinister significance, because clinical observation has shown that squamous-celled cancer is very liable to arise at the edges of such patches, or in the deep fissures which sometimes traverse them.

In 1895, when I became surgeon to the Chelsea Hospital for Women and thus had excellent opportunities for observing diseases of the vulva, I noticed in many of the patients who came complaining of vulval irritation that some of the cases, which would be classed on cursory examination as examples of kraurosis, presented appearances which, had they been situated on the lingual or buccal mucous membrane,

would be called leukoplakia. Subsequently I satisfied myself that this condition is identical with lingual leukoplakia, and like it is often the forerunner of squamous-celled cancer.

I drew attention to the matter in a book which I published on 'Diseases of Women' with the assistance of Dr. A. E. Giles in 1897 (p. 86). Since that date other surgeons have published reports of cases of cancer of the vulva showing the close association of the two conditions. In my early observations I held the opinion that in all probability syphilis was the cause of vulvar leukoplakia, but more extensive observations have convinced me that it occurs independently of this disease. It is worth mention that Bonney has made a careful histological investigation of vulvar leukoplakia, which shows that the changes in the epithelial and subepithelial tissues are identical with those produced by this pathological condition in the tongue ('Archives of the Middlesex Hospital,' vol. xiii, Seventh Report from the Clinical Research Laboratories).

CARCINOMA OF THE VULVA.

In discussing cancer of the lip I mentioned to you that in the years 1897-1907, both years inclusive, fifty cases of cancer of the lip (all men) were admitted into the surgical ward of this hospital. Dr. Comyns Berkeley informs me that in the decade 1898-1908 there were fifty-seven women admitted into this hospital and the Chelsea Hospital for Women with carcinoma of the vulva, and that in all the patients the inner surfaces of the labia majora presented the condition known as kraurosis, or leukoplakia. When the social histories of these women are analysed they are instructive, because among these fifty-seven patients there were fifteen widows, thirty-four married women, and eight spinsters. These observations indicate that

trauma connected with coition and childbirth are probably factors in producing the changes which render the epithelial tissues of the vulva liable to cancer. I have satisfied myself that some of the patients were syphilitic.

It is a significant feature in relation to vulvar cancer that trauma connected with the sexual act and its results plays the same part in connection with the labia that the habit of smoking short, dirty clay pipes exercises on the mucous membrane of the lips.

Cancer of the labia has many features in common with cancer of the lip. For example, it may arise in any part of the internal surface of a labium and destroy it, implicate the underlying tissues, and quickly infect the inguinal lymph-glands of the corresponding side. In some cases it arises in the angle between the greater and lesser labium, near the anterior part, and then extends into the tissues which form the cutaneous hood of the clitoris and implicates the labium of the opposite side, in the same manner that cancer arising in the lower lip near the angle of the mouth will creep around the commissure and involve the upper lip, but there is this difference in the case of the labia: when the carcinoma spreads across the median fold into the opposite labium, the lymph-glands in both groins will become cancerous. It occasionally happens that cancer arises in the cutaneous hood of the clitoris, and in such circumstances it may be, and is sometimes, mistaken for carcinoma of the clitoris. It is essential to look carefully into the precise relations of the cancerous ulcer to the labia, and it is worth while to note carefully when there is a large cancerous ulcer on one labium and another ulcer at a corresponding spot on the opposite labium, to determine, if possible, whether the two are connected by a band of cancerous infiltration either over the clitoris or across the vestibule, for it is maintained by some surgeons that when

two cancerous ulcers exist in corresponding spots on opposed surfaces of the greater labia, that in some instances at least one of the ulcers is due to infection from the contact of a healthy labium with a cancerous ulcer on its fellow. Reputed instances of this are numerous, but when the facts are submitted to a critical inquiry few stand the test.

Cancer of the labium has an age-incidence which corresponds fairly with that for the lip, and it is probable that this disease is as common in women as is cancer of the lip in men. The disease runs a similar course, and as it involves the urinary meatus, and sometimes the anus, it leads to great distress in its late stages, and reduces its victims to a miserable condition.

From an operative point of view the results of the free and wide removal of the infected parts give excellent results if seen early. The wounds made by the operation heal quickly, and I find it a great advantage to remove the primary disease at the first operation, and fourteen days later when the parts are healed to thoroughly extirpate the lymph-glands in both groins. In removing the labia the surgeon takes care not to damage the urinary meatus. The precise method of dealing with the tissues surrounding this orifice varies according to the extent of the operation, but it is a matter which rarely causes difficulty. The complete extirpation of the lymph-glands in the groin in these circumstances is in keeping with the surgical measures employed against cancer of the lips.

It appears to me clear from a consideration, as well as a comparison, of the conditions surrounding cancer of the lips and of the vulva, that trauma plays a significant part in rendering the epithelium investing the lips and labia vulnerable to the parasite of cancer, inasmuch as frequently repeated injuries maintain the parts in a condition of chronic inflammation.

THE NATURAL HISTORY OF CANCER OF THE UTERUS.

X.

ON reviewing the facts relating to cancer of the various organs which we have considered in the preceding discourses, it was clearly set out that the leading features of this widespread and destructive disease are : its undoubted origin in epithelial cells, its insidiousness, its invasiveness, and its proneness to attack organs the seat of chronic disease. To these must be added the tendency of cancer to infect lymph-glands, and to disseminate, producing secondary growths in distant parts of the body, the massiveness of the secondary growths being often in striking contrast to the size of the primary cancer. The lethal effect of the disease is considerably retarded or accelerated according to the environment of the organ primarily affected.

A study of the natural history of cancer when it attacks the uterus is brimful of instruction in regard to these matters ; and you will have ample opportunities of studying them, for patients with cancer of the uterus abound in this hospital.

In regard to the epithelial investment of the uterus, let me remind you that the endometrium of the cervical canal and the body of the uterus is lined with columnar epithelium, which is continued through the Fallopian tube to end at its coelomic ostium, where there is an abrupt transition to the pavement-like epithelium (endothelium) of the peritoneum. The epithelium of

the cervical endometrium undergoes a simple transformation at the external mouth (or *os*) of the uterus into the stratified or squamous-celled type, which lines the surface of the vaginal mucous membrane. The portion of the cervix uteri which projects into the vagina receives, by invagination, a covering of vaginal mucous membrane; the boundary line between the squamous cells belonging to the vaginal investment and the columnar cells which clothe the walls of the cervical canal is situated, in a healthy woman, at the margin of the external *os*. It is necessary also to remind you that the epithelium of the uterus lines the glands of the endometrium, and, in the case of the cavity of the uterus and the Fallopian tubes, the columnar cells are ciliated.

Cancer may attack any portion of this epithelial tract, from the squamous cells investing the vaginal portion of the neck of the uterus up to its termination at the peritoneal margin of the tubal ostium. The vulnerability of the epithelium so far as cancer is concerned varies very greatly in the various parts. Cancer in the cervical segment is dreadfully common, in the uterine cavity less frequent, and in the Fallopian tube rare. Its presence in the tubes was unknown, indeed, even unsuspected, before 1880. The relative liability of these three sections of the genital tract to primary cancer may be represented in this way. If the liability of the cervix be represented by five hundred, that of the body of the uterus would be twenty-five, and the Fallopian tube one. These comparisons are very striking even in the face of the fact that when cancer arises on the vaginal surface of the cervix, it is classed with those cases which arise in the epithelium of the cervical canal, whereas in the strict anatomical sense it belongs to the vagina. This is a matter which requires further notice because primary cancer of the vaginal mucous membrane is uncommon

or rare. Strictly, the vaginal mucous membrane ends at the margin of the os uteri, and cancer arising in the epithelial investment of that portion of the cervix uteri which is capped with squamous epithelium should, as I have already remarked, be classed with vaginal cancers, but from the clinical point of view it would be an unpractical arrangement. Similarly, when cancer arises in the section of the vagina adjacent to the vulva it will involve the vulval mucous membrane, and when well established it is difficult to determine whether the disease arose in the mucous membrane of the vulva or the vagina. Thus it comes about that, speaking generally, the only examples of cancer arising in the vaginal mucous membrane which run no risk of being classed as vulval, or uterine, are those originating in the middle segment of this mucous canal.

Cancer of the vagina is rare; for example, in the quinquennium 1904-8 three patients with cancer of the vagina died in the Middlesex Hospital. During the same period it is stated in 'The Eighth Report of the Cancer Research Laboratories' that 241 women with cancer of the neck of the uterus were admitted in the general wards and in the cancer asylum.

When we come to analyse the "social state" (as our registrars call it) of these women with cancer of the neck of the uterus, we find this disease especially common in woman who have borne children, and disappointing as it may seem, fecundity increases their liability. Critical inquiry shows that injury (trauma) associated with coition and childbirth, but more particularly the latter, is a potent factor in producing the changes which render the epithelial tissues in this situation liable to cancer. This has already been pointed out in relation to primary cancer of the vulva (see Lecture IX). For ten years I devoted particular attention to this aspect of cancer of the cervix, and during the whole of that time whenever

an example of this disease came under my notice in a woman who had never been pregnant I took unusual pains to satisfy myself that the morbid condition of the cervix was clearly cancer, and whenever possible a fragment of the affected tissue was removed and submitted to microscopical examination. In several instances the naked-eye diagnosis of cancer was discredited, the cancer-like tissue proved to be of the nature of granulation tissue in several instances, in a few it was exuberant glandular tissue, and in one tuberculous. One woman had such a suspicious condition of the cervix uteri, and though a microscopic examination of the growth left its nature in doubt, I advised the patient to submit to vaginal hysterectomy. The operation was carried out, and quite by accident she came under my care again after an interval of nine years for piles; she had remained in excellent health during the whole of that period. Many other examples of suspected cancer of the cervix which have remained free from recurrence after removal of the cervix or complete extirpation of the uterus come into this category. On one occasion a harlot, aged twenty-five years, came under my observation with a lesion of the cervix which appeared to be cancerous; all who saw it were satisfied that the lesion was malignant. I was not so sure about it; the age of the patient, and the fact that she had never conceived weighed in my mind against cancer, so instead of removing the uterus I cut off the vaginal portion of the cervix and divided it into three pieces; I bestowed a piece on two competent histologists and kept one myself for examination. The histologists decided that the disease was cancerous, and in deference to this opinion I completely removed the uterus. Five years later the patient reported herself in excellent health. Reflecting on such experiences, I cannot help coming to the conclusion that where there is diagnostic doubt the disease is set down as cancer when it is

really inflammatory or of infective origin. If every case reported as cancer of the neck of the uterus which occurs in virgin-spinsters is submitted to rigorous diagnostic tests, supported by a careful microscopic examination of the tissue, I feel sure that these patients will only form about 1 per cent. of the total.

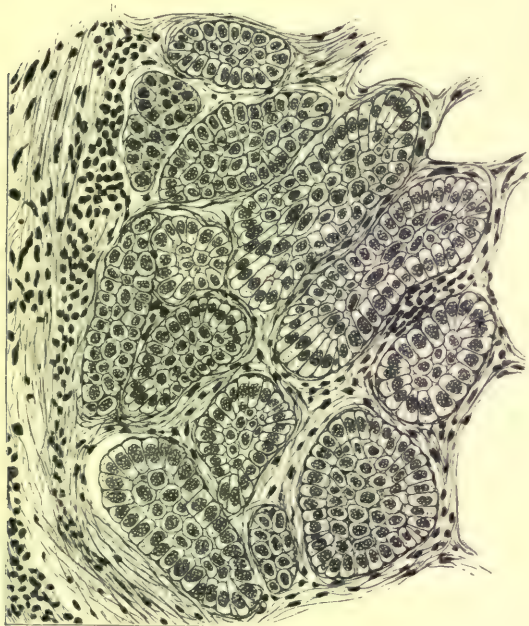


FIG. 19.—The microscopic characters of cancer arising in the neck of the uterus.

In dealing with cancer of the vulva (Lecture IX) mention was made of the leucoplakic condition often seen on the inner surface of the labia and of its significance as a precursor of cancer. A similar change is sometimes seen on the neck of the uterus; I have observed it, but the common morbid condition which not only precedes cancer of the neck of the uterus, but which when severe is often mistaken for it, is the mor-

bid condition which used to be called "ulceration of the cervix" or "erosion," until Ruge and Veit (1878) showed that the soft pink tissue was not due to ulceration, but consists of an overgrowth of the glandular tissue of the cervical canal which over-runs the cervix uteri around its "os." The difference in the structure of cancer and the pink adenomatous tissue, so common around the mouth of the uterus, is shown in Figs. 19 and 20.



FIG. 20.—The microscopical features of the pink tissue at the neck of the uterus commonly called "an erosion." (After Bonney.)

A common sequel to childbirth is laceration of the neck of the uterus, and in multiparous women it is often disfigured by fissures radiating in various directions from the os, and in the recesses of these fissures you find collections of this strawberry-pink tissue. The opinion is strongly held by many thoughtful men that these fissures, and especially the glandular tissue connected with it, constitute a precancerous condition. The changes are often termed "cervicitis" for clinical

convenience, and recent investigations on the early stages of cancer arising in the cervix uteri unanimously support the views that cervicitis and glandular changes are pre-existent in all cases. The precise cause of these chronic changes has not been identified, but it must be something peculiar; certainly the history of women who come under observation with long-retained pessaries shows that something more than long-continued irritation, ulceration and dirt is necessary for the production of cancer in the neck of the uterus. It is also a fact that women are occasionally brought to us in consultation under the impression that they are suffering from advanced cancer of the uterus, and on examination a forgotten pessary is discovered. A remarkable case of this kind happened to me in 1908. A Jewess, aged sixty-five years, and diabetic, had a carcinoma in her right breast. Arrangements were made for its removal, and on the morning of the operation the nurse told me that the patient had a foul vaginal discharge. The doctor thought it might be due to uterine cancer secondary to the disease in the breast. I expressed the opinion that it probably depended on a forgotten pessary. I removed the breast and dressed it carefully, and then examined the vagina and extracted a vulcanite pessary. The stench may be imagined, but it was indescribable. Later we ascertained that the pessary had been in the vagina twenty-seven years; the patient assured us that she would never allow anyone to remove it. It is true that Dr. F. J. McCann has observed an example of primary cancer of the vagina associated with a pessary. A woman, aged seventy years, had worn a ring pessary for four years without removing it. When she came under observation a ring-shaped cancerous growth was found in that portion of the vaginal mucous membrane which came in contact with the pessary. No one has attributed any malicious influence to vaginal pessaries so far as cancer is concerned. As has been

mentioned already, cancer of the vagina is rare but the use of pessaries extremely common. In 1902 I attempted to collect some statistics in regard to pessaries. One London maker stated that he supplied ten thousand rubber rings and globular pessaries, and three thousand vulcanite "Hodges" annually. Another supplied the trade with thirty-six thousand yearly, and added, "vast quantities of pessaries are imported from Germany and other countries." There are several makers of pessaries in London, so that you will be able to form some notion concerning the frequency with which they are employed. Though the persistent use of a pessary is not favourable to cleanliness, it cannot be charged with causing cancer.

Cancer of the Body of the Uterus.—The consideration of cancer arising in the epithelium lining the cavity of the uterus proper proves that the social state of the patient plays here a part as conspicuous as in the case of the cervix. At first sight it may seem to you somewhat arbitrary to divide uterine cancer into two classes according to its situation in the neck, or in the body of the organ, but this arrangement is well justified. It is undeniable that cancer may arise in the uterine epithelium at any point from the external os to the fundus uteri; it is, nevertheless, uncommon to find a primary cancer in the endometrium of that part of the canal which traverses what is well known as the supra-vaginal section of the cervix uteri; when it arises in this section it is a very insidious and treacherous form of the disease. The remarkable feature in regard to cancer when it arises in the epithelium of the corporeal endothelium, or, as it is termed in clinical phraseology, "cancer of the body of the uterus," is the reverse of the conditions surrounding its ætiology when it affects the neck of this organ, for it is more common in virgin-spinsters and barren married women than in mothers.

Our knowledge of cancer of the corporeal endo-

metrium is of fairly recent date. Twenty years ago it was regarded as an uncommon disease, but since hysterectomy as a radical method of treating obstinate uterine disease has come to be more freely and safely practised, we have acquired some accurate knowledge in consequence. This new knowledge has served to establish the fact that cancer in this situation is more frequent in childless women and aged spinsters than in fertile women; it also shows that it is commoner at the menopause than at any other period, whereas cancer of the cervix is especially common between the fortieth and fiftieth years of life. Accurate pathological investigations of the corporeal endometrium have shown that there are some epithelial perversions in this tissue which mimic very closely cancerous formations, and in some instances predispose to them. To my mind the most noteworthy observations in this field are those of Piquand. In 1905 he drew attention to the frequency with which a submucous fibroid was associated with cancer of the corporeal endometrium, especially in women of fifty years and upwards. In this connection he also emphasised what other observers had pointed out, namely, that a submucous fibroid is usually associated with changes in the endometrium, which not only cause excessive bleeding, but set up inflammatory changes, giving rise to leucorrhœa, salpingitis, pyosalpinx, and such changes in the epithelium as render it susceptible to cancer. Piquand's statistics support his views. I have examined my own cases in the light of his statements, and the result may be briefly expressed in this way: That among women submitted to hysterectomy for fibroids over the age of fifty years, about 10 per cent. of them will have cancer of the corporeal endometrium. Kelly and Cullen, among 1674 cases of hysterectomy for fibroids, found twenty-three examples of carcinoma of the body of the uterus. If these conclusions are confirmed by other observers, the

suspicion that submucous fibroids predispose to cancer will be transformed into a grim reality, and warn practitioners of the dangers of allowing the disease to drift into an inoperable condition simply because the patient has attained the age of the menopause. There is another perversion of the uterine epithelium often overlooked in less pronounced examples, whilst in extreme cases it is apt to be mistaken for cancer of

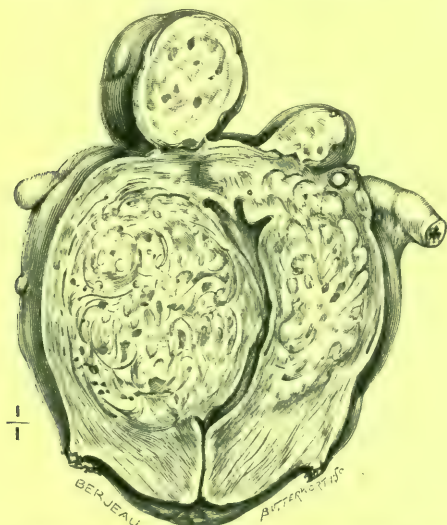


FIG. 21.—A small uterus with diffuse adenomyoma from a barren married woman. The uterus is represented in coronal section.

the body of the uterus, namely, the morbid condition known as diffuse adenomyoma of the uterus. Indeed, there is reason to believe that exceptionally it terminates in cancer. From a careful examination of some specimens described as adeno-carcinoma of the body of the uterus, I have come to the opinion that some cases so described were really examples of diffuse adenomyoma. This disease, like cancer, may arise even in small, atrophic uteri (Figs. 21 and 22).

An interesting feature of this disease is the frequency

with which uteri attacked by it show traces of antecedent inflammation, for not only are the Fallopian tubes frequently thickened and their cœlomic ostia occluded, but the uterus itself is often firmly adherent to the bladder, rectum, intestines and adjacent peritoneum. Diffuse adenomyoma not only simulates the symptoms and physical signs of cancer of the body of the uterus, but it may be in itself a pre-cancerous condition.

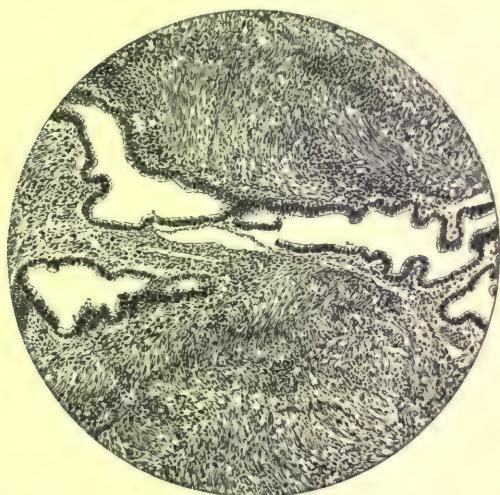


FIG. 22.—Microscopical features of diffuse adenomyoma of the uterus. $\times 60$. (After Frank E. Taylor.)

Concerning the early stages of uterine cancer we know little, but we know more of the beginnings of this disease in the neck than in the body of the organ. A careful and regular attendance at a gynæcological clinique in any large British city or town will soon satisfy an observant student that cancer of the cervix uteri begins in a fissure left by the healing of a laceration following child-birth, or as a circular ulcer with raised edges, or in an exuberant papillomatous form. The ulcerating type is common,

the exuberant form rare. The mode in which the disease begins in the cervix is a parallel of its beginnings on the edge of the lower lip. So far as the early stages of cancer arising in the corporeal endometrium are concerned, very little derived from actual observation is forthcoming, but what we know of the disease when well advanced is sufficient to enable me to tell you that there is an ulcerating, and there is an exuberant or massive form. In regard to these I shall have something to say later, but let me here state that on two occasions only has it fallen to my lot to see primary cancer of the corporeal endometrium in such an early stage that the disease was limited to the superficial layers of the endometrium.

In all parts of the body there is often great difficulty in determining from a clinical examination whether in a given case the patient is suffering from cancer, a simple tumour, or an inflammatory swelling; moreover, the employment of the microscope will not always decide. There is no certain sign of cancer. The uterus is no exception to this rule, as the following case serves to show: A multipara, aged eighty-three years, complained of uterine bleeding for which she was examined under an anæsthetic; fragments from the uterine cavity were secured by a curette, and after a careful microscopic examination were pronounced to be cancerous. The age of the patient was held to be a bar to hysterectomy. She came under my care; as the old lady appeared to be otherwise in good health I decided to remove the uterus. Vaginal hysterectomy was performed, and on examining the soft growth which filled the uterine cavity I found that it resembled in every particular the villous papillomata so common in the urinary bladder (Fig. 23). This view of the microscopic characters of the growth was confirmed by a committee of the Obstetrical Society, which critically examined and reported on

the specimen (see 'Trans. Obstet. Soc., London,' vol. xlix, pp. 46, 93). The correctness of this opinion is supported by the fact that three years after the operation the patient was said to be in good health (September, 1909).

Let me also draw your attention strongly to the fact

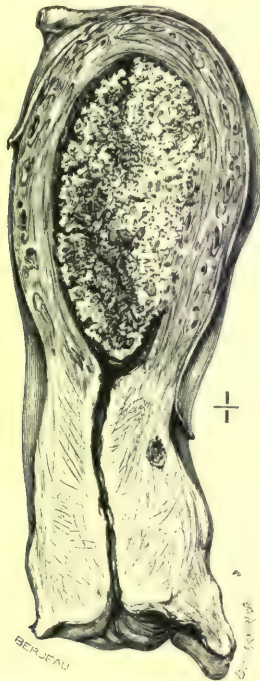


FIG. 23.—A uterus with villous disease of the endometrium.
Removed from a multipara, aged eighty-three years.

that cancer of the body of the uterus occurs in aged spinsters and barren wives, women in whom the uterus after the forty-fifth year is below the average size, unless it happens to contain fibroids. The corporeal endometrium of such atrophic uteri occasionally becomes the seat of cancer, and it is very likely to be overlooked, and this for two reasons: the chief one is due to the

fact that the vagina is so extremely narrow that it prevents an adequate examination, and in patients in whom it can be carried out the uterus is found to be so small that the possibility of cancer being present is not entertained.

I want to impress on your minds very carefully that the size of a uterus is no guide in the diagnosis of cancer of the corporeal endometrium; I have found a uterus cancerous when the whole organ scarcely exceeded the dimensions of a man's thumb, and I have seen one so stuffed with cancer that it reached the navel. Observation teaches that cancer of the corporeal endometrium of an atropic uterus is of a low degree of malignancy.

Variations in Malignancy.—There is a clinical feature of uterine cancer, whether it attacks the neck or the body of the organ, which is not thoroughly appreciated: I refer to variations in its malignancy. We do not sufficiently realise that cancer may arise in the uterus and destroy the patient's life in twelve months. Many untreated cases run on for two, three, and even four years, and in the case of the body of the uterus for much longer periods. Cancer, it is true, varies widely in its malignancy in nearly all the situations in which it grows. Cancer of the breast in a suckling woman will run its deadly course in a few months, but in an older woman it may require ten, twelve, and even twenty years to destroy the patient. Cancer of the cæcum will in exceptional cases grow so slowly as to require five, and even seven years, to kill its victim, and the same is true of cancer of the rectum.

Cancer and Sepsis.—As a rule, cancer of the neck of the uterus runs its course more rapidly than the same disease inside the uterus, but this is due to an accidental circumstance, namely, the rapidity with which a cancerous cervix becomes septic. This is a matter of great importance.

An innocent differs from a malignant tumour in the possession of an investing capsule, and as long as it remains intact the tumour is protected from pathogenic micro-organisms. When the capsule is injured, or sloughs, infecting agents gain access to the tumour-tissue, causing general disturbance of the patient's health. Cancer possesses no capsule, and as a rule is situated on epithelial surfaces where it is exposed to micro-organisms, for example, the lips, the gullet, tongue, larynx, stomach, intestines, and cutaneous surfaces. The exuberant tissue formed by the growth of the cancer being poor in blood-vessels, and therefore of low vitality, is easily infected by pathogenic micro-organisms and decomposes; the products of these changes are cast off as offensive discharges, the infective agents gain access to the blood-stream, set up general disturbance of the patient's health, and produce the peculiar sallow complexion which used to be termed the "cancerous cachexia," but which is in reality due to the absorption of the products—toxins—brewed by the micro-organisms.

In the case of cancer of the tongue this condition of things is so well recognised that surgeons, in preparing patients for removal of a cancerous tongue, knowing full well the dangers they run from sepsis due to swallowing, as well as the inhalation of the germ-laden and therefore septic discharges from the ulcerated surface, do their best to render the individual immune by vaccinating him with a prophylactic serum.

It is noteworthy that, as a rule, those cancers run the most rapid course which are situated in positions most accessible to pathogenic micro-organisms. The tongue and larynx are good examples, but probably in no other situation in the body can this be so strikingly demonstrated as in the uterus. Cancer in the cervix becomes septic more rapidly than cancer within the uterus, and the modes by which this disease destroys

life in these two situations differ in some very important particulars. Before proceeding to discuss these points it is also necessary to remind you that cancer of the same organ shows marked differences in malignancy in different individuals.

Until menstruation is established the vagina and the uterine cavity are to be regarded as functionless canals, and in virgins they are practically air-tight. After marriage and child-birth, air, and therefore micro-organisms, obtain access to the vaginal passage and the vaginal portion of the uterine cervix; consequently when the cervix is attacked by cancer, the morbid tissue is as liable to decompose as when cancer attacks the tongue. It is the accession of septic changes in this cancerous tissue which causes cancer of the neck of the uterus to be such a distressing disease, for as the ulceration extends to, and opens up adjacent viscera, such as the bladder and the rectum, it also involves the ureters, leading to septic infections of the whole urinary tract. The extensive ulceration and sloughing of uterine, vaginal and rectal tissue which is such a well-known feature of this disease, is greatly promoted by the septic infection. Indeed, it may be stated that the death of patients affected with cancer of the uterus is mainly brought about by sepsis. Chief among these terminal infections are uræmia and peritonitis, the latter being due to perforation of the wall, or actual leakage of purulent fluid from the Fallopian tubes, which become distended with infective fluid, secondary to the accumulation of septic material in the uterine cavity. In a small proportion of cases, probably 6 per cent., the uterus is in the condition known as pyometra, and in exceptional instances the septic fluid pent up in the uterine cavity leaks through a hole caused by ulceration in the uterine wall. Thrombosis of the iliac veins is not uncommon, and its sequelæ, gangrene and pulmonary embolism. Uræmia is the

most frequent of all the terminal infections which occur in women with cancer of the cervix uteri; it is due to the implication of the vesical segments of the ureters and the bladder (Fig. 24). Those who have carefully carried out systematic examinations of patients who have died from cancer of the cervix uteri draw attention to the frequency with which dilatation of the ureters and the renal pelves is found. Indeed, some observers fix the frequency of ureteral and renal complications in this disease as high as 70 per cent.

Without accepting this high proportion of renal complications, no one who has had opportunities of following cases of cancer of the cervix to their termination can doubt that uræmic symptoms are present in the majority of these patients. (It may be mentioned here that cancer of the rectum in women and men frequently destroys its victims by uræmia and anuria, caused by the bladder and the ureters being implicated by the cancer.) This unhappy picture does not end here; it is the presence of septic micro-organisms in this cancerous tissue which makes the efforts of the surgeon approach in some measure to the labour of Sisyphus. If you study carefully the results of the earnest and praiseworthy efforts now being made to relieve, by surgical means, women suffering from cancer of the neck of the uterus, you will find that it is not the technical difficulties which baffle the surgeons, it is the difficulty of controlling the sepsis; it is this which accounts for the high mortality of what is known as the radical operation for cancer of the cervix, and among the various micro-organisms which lurk in cancerous tissues the virulent streptococcus is frequently found. It is true that most surgeons, as a preliminary to such operations, remove by scraping and cauterising the redundant and infected tissue, but it is time they followed the practice mentioned in regard to the treatment of cancerous tongues, and attempt to control these

micro-organisms by a vaccine before resorting to hysterectomy.

Another feature which cancer of the neck of the uterus shares with cancer of the tongue is the infrequency of secondary deposits. Dissemination of cancer

Ovary infiltrated with cancer.

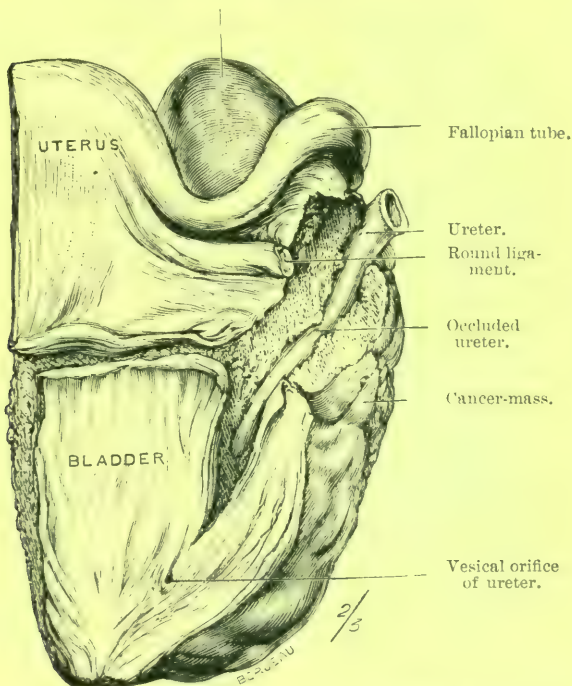


FIG. 24.—Cancer of the neck of the uterus implicating the ureter.

is a slow process, and in those situations where this disease kills comparatively quickly as a consequence of septic complication, secondary deposits are few in number, small in size, and only obvious in a small proportion of cases. In cancer of the tongue the adjacent lymph-glands quickly enlarge; this is not the case in cancer of the cervix, indeed, some careful investigations

show that in the bodies of patients in whom the disease has run its fatal course, enlarged lymph-glands are found in about half the cases, and it is a fair computation that among the women who are submitted to hysterectomy for cancer of the uterus, in about one third of the number the lymph-glands in the pelvic and lumbar regions will be enlarged. It is important also to remember that because a pelvic lymph-gland is enlarged in a patient with cervical cancer it must not be assumed that the increase in size is due to cancerous infection. A careful microscopic examination will often prove that it is due to inflammatory changes. It cannot be too strongly impressed on your minds that there is no certain means of determining clinically whether an enlarged lymph-gland is cancerous or not without a microscopic examination. Hardness is no test; a very soft gland may be full of cancer-cells, and this is a matter of some practical importance, because in removing lymph-glands stuffed with cancer-cells, especially if they be roughly handled, the capsules of the glands will break, and the cells escape and lodge in the connective-tissue surfaces exposed during the manipulations; these cells grow and form new masses of cancer. This is known as "cancer infection"; I have often drawn attention to its occurrence after extensive operations for cancer, and it is a frequent cause of failure (see especially Lecture III), and it is a noteworthy fact, to which Comyns Berkeley has recently drawn attention, that in cases of radical hysterectomy for cancer of the neck of the uterus, where the removal of enlarged lymph-glands forms a prominent feature of the operation, quick recurrence is the rule.

A comparison of the course of cancer arising inside the uterus with that of cancer originating in the cervix will serve to illustrate the part played by pathogenic organisms in shortening the duration of the disease. It has already been mentioned that the uterine cavity in

virgin-spinsters and barren women is practically an airtight chamber, and that cancer of the corporeal endometrium is more prone to arise in sterile women than in those who are fertile. When cancer arises in the body of the uterus of a multiparous woman—a rare occurrence—the cervical canal is patent and occasionally septic. In such an event the disease assumes the form of a destructive cancerous ulcer, such as we are familiar with in the cervix. When cancer arises in the corporeal endometrium of a barren uterus with a narrow cervical canal it assumes the massive form. Take, for instance, the specimen represented in Fig. 25: the uterus is enlarged to nearly thrice its ordinary size; its cavity contains an unencapsuled mass of cancerous tissue; its walls are thin, due to the slow expanding force exercised by the persistent growing mass within. If you examine the specimen critically, an outrunner from the cancerous mass will be seen creeping down the cervical canal, and the tip of it emerges through the mouth of the womb as a slough. This uterus was removed from a spinster, aged fifty-six years, on account of irregular hæmorrhages. It is clear from an examination of the specimen that the cancerous mass had been growing within the uterus without causing symptoms until the tongue-like piece of growth protruding from the os uteri became septic; then she became conscious of bleeding, and this eventually led to the detection of the disease within the uterus.

Some of you may ask, and with reason, what changes would have happened in the uterus had the disease remained undetected? This is not difficult to answer. I have already mentioned that when pathogenic micro-organisms invade cancerous masses they cause it to decompose and slough (the fragments escaping with the foetid discharges which constitute such a disagreeable and often disgusting feature of the late stages of uterine cancer). The patient thus

becomes exhausted by a combination of general septic infection and recurrent uterine hæmorrhages. There is another way in which cancer of the corporeal endometrium causes death. Cancer-cells possess the dangerous property of eroding tissues with which they are in contact. This invasiveness of cancer-cells in the case of the uterus leads them to permeate and



FIG. 25.—A cancerous uterus in coronal section. The cancer is of the massive kind. From a spinster, aged fifty-six years.

penetrate its muscular walls, and the cells escaping into the belly, engraft themselves on the walls of any organs, such as intestine, ovary, or omentum, which may happen to be in its vicinity. In some cases the cancerous process may appear as a small “bud” on the serous surface of the uterus. In the woman from whom the uterus and bladder represented in Fig. 26 were taken, the peritoneal investment of the abdominal viscera presented minute cancerous nodules in

thousands. Rarely the cancerous mass may form a boss on the fundus of the uterus as big as a golf-ball (Fig. 27).

I am anxious to impress upon you in regard to this matter an important fact; it is this: A primary cancer of the body of the uterus may completely permeate the muscular tissue of the fundus and fail to produce



FIG. 26.—Cancerous uterus in sagittal section. A bud-like process of cancer has eroded the uterine wall and protrudes on the peritoneal surface. The peritoneum was dotted with thousands of secondary nodules.

any irregularity in the contour of its serous surface, but in spite of this the general peritoneal cavity may be seriously infected. I performed hysterectomy on a spinster, aged sixty years, on account of menorrhagia, which was attributed to a submucous fibroid. The uterus was removed, and before closing the abdominal incision I looked carefully around, and caught sight of a flattened discoid mass, 10 cm. in diameter, lying

in the great omentum ; it was removed. This mass and the uterus were hardened, and two weeks later the omental tumour was examined microscopically and found to be a secondary deposit of cancer. I at once bisected



FIG. 27.—A uterus in sagittal section. The endometrium is cancerous, and the disease has involved the muscular tissue and formed a large knob on the fundus of the organ.

the uterus, and found that it contained a submucuous fibroid, and the uterine cavity contained a quantity of soft cancerous material. We at once realised that the cancer had become extensively generalised in the belly to produce such a large lump in the omentum, and that the outlook for the patient was bad. She died

with extensive abdominal recurrence four months after the operation. This case shows well what an insidious process cancerous permeation is—slow, persistent, and painless. In this case there was nothing on the peritoneal aspect of the uterus, and nothing to be seen on the pelvic peritoneum, and no enlargement of the pelvic and lumbar lymph-glands to lead me to suspect that the peritoneum was thoroughly infected with cancer-cells. The only symptom of which the patient complained was irregular losses of blood from the vagina, and the only physical sign was an enlargement of the body of the uterus. Pain and tenderness were absent.

You should remember these facts, because you will from time to time hear a gynæcologist exclaim on examining a woman with advanced cancer of the uterus: "What a pity you did not seek my aid earlier!" Do not imitate this. You will unfortunately see many similar cases when you practise the art of gynæcology. Do not upbraid the patient; she has no idea when she consults a doctor that her uterus is cancerous, and even when such women come for advice in the early and doubtful stages, practitioners lack the courage to advise a serious operation when diagnosis is uncertain.

The idea of instructing women by issuing pamphlets concerning the early stages of uterine cancer is to fill their minds with fear. It seems to me that a propaganda of this kind only serves to add another terror to the life of suffering woman.

TRAUMA IN RELATION TO MALIGNANT TUMOURS.

XI.

TWENTY years ago I made a very careful study of the writings relating to the causation of tumours, as well as a practical personal inquiry, which enabled me to satisfy myself that no convincing facts were forthcoming in support of the view that direct injury led to the formation of a carcinoma. The matter has, however, become important in consequence of a recent Act of Parliament, which extends the scope of workpeople and servants injured in the course of their employment for recovering damages from their employers. As a result, cases have already been brought into courts of law for the purpose of recovering damages for malignant tumours attributed to bodily injury sustained in the course of employment, and in at least one case such a claim has been successful.

When you come to practise your profession you will quickly learn, if you have not already appreciated the fact whilst attending the out-patient rooms and wards of the hospital, that men and women almost invariably endeavour to associate a local ailment with a local cause, and this is especially true in regard to tumours of the limbs and breasts. Patients will remark sometimes in regard to an obvious tumour for which they seek advice, "I cannot account for it in any way, for I don't ever remember knocking myself there," as if it were part of their duty as a preliminary when seeking

advice, to rummage their minds for a recollection of some antecedent injury.

So far as carcinoma is concerned, trauma as an ætiological factor has only been seriously advanced in the case of the breast, and it is in regard to this organ that I propose to consider the matter in detail on the present occasion.

The breast is liable to two kinds of malignant disease—carcinoma and sarcoma. The former arises in the epithelium lining the ducts and acini of the glandular elements of the breast, whilst the latter arises in its connective tissue (see Lecture II).

Cancer of the breast is a common disease; indeed, this organ shares with the stomach and the uterus the distinction of being the most common situations in which this disease occurs primarily. Sarcoma of the breast is an uncommon disease, and from the comparison of a number of statistical papers devoted to this matter it may be fairly stated that, out of every hundred cases of malignant disease of the breast, ninety are carcinoma and the remainder some form of sarcoma. It may also be mentioned here that these two forms of malignant disease attack the male breast. Most surgeons will agree with me in the statement that malignant disease is one hundred times more common in the breasts of women than in the breasts of men. Cancer arising concurrently in both breasts is unusual: its frequency is variously estimated by different observers at from 1 to 2 per cent. The liability of the right and left breast to become attacked by cancer is equal.

The breast, like other superficial parts of the body, is liable to injury in the form of blows, knocks, and stabs, and it may be bruised when a woman falls on her breast or knocks it against hard bodies, like bed-posts and the corners of furniture; it is sometimes injured by hard bodies hurled through the air, such as

bricks, stones, or books. A common form of accident is a blow on the breast from an elbow in a struggle or in a crowd; brutal men inflict serious injuries on this part of women by blows with the fists, and even kicks. Street accidents constitute another common class of injury, such as being run over by vehicles, or kicked by horses. Nursemaids often complain of being thumped on the breast by unruly children, and those who are engaged in hard work receive accidental blows from broom-handles, and other forms of hand implements, or from machinery. Pressure from hard corsets has often been blamed for injuring the breasts.

In the out-patient room of a general hospital a large number of women are treated annually for injuries to the breast. When the breast is injured it bleeds like other parts of the body, and as the mammary tissues are soft the blood sometimes infiltrates them freely, producing the usual purple staining of the skin, familiarly known as a bruise. Many slight injuries of the breast, although they cause great pain (for the tenderness of the breast is proverbial), are not accompanied by any staining of the skin, although there may be an effusion of blood in the deeper tissues.

In the majority of cases the effused blood slowly absorbs, but if much blood has been discharged into the tissues there remains, sometimes for many months, a hardened area with indefinite outlines in the tissues of the breast, and this small indurated area is sometimes supposed to be the starting-point of cancer.

It may be assumed that blows and similar severe mechanical insults to such a delicate organ as the breast, cause so much pain and leave such an impression on the mind of the sufferer that it is rarely forgotten. A definite proportion of women with cancerous breasts, which amounts to at least 10 per cent., will state unasked that they have received an injury to the breast. In some the blow occurred a few months

previously, in others as much as thirty years before. A few, if closely questioned, will recall to mind an injury received some years previously.

There can be little doubt that the majority of women have received at some period of their lives a knock upon their breasts, and that the frequency with which women attribute the cause of a cancerous tumour within the breast to an injury is largely due to the belief, deeply rooted in their minds, that such injuries are the common cause of cancer, and though 10 per cent. of patients with this disease in their breast can, and do, assign a specific injury as the starting-point, it is probably true that not 1 per 1000 of women who have received a severe blow on the breast becomes the victim of cancer. With men it is different, for in them the ratio of an intensive injury as a forerunner of malignant tumours of the breast is much higher than in women, although cancer of the male breast is in the proportion of 1 to 100 in women.

It should be remembered that many lumps in the breast, supposed to be cancerous when merely examined by the eye and fingers, prove to be non-malignant when examined microscopically. Although surgeons have been looking at tumours of the breast since the days of Hippocrates, and even before that, yet to-day there is no unequivocal sign by which cancer may be recognised. In the early stages of this disease a hard, irregular, indefinitely circumscribed lump is felt in the breast, and is, as a rule, painless. In many instances the wisest and most experienced surgeons cannot be certain whether the lump is cancerous, or due to chronic inflammation of the true mammary tissue (mastitis), a tumour of the glandular tissue (a fibroadenoma), or a dilatation of one of the ducts (a cyst), or a specific infection, such as is found in syphilis, or tubercle, and sometimes an abscess.

Age is of some assistance in the diagnosis of uncertain

lumps in the breast. No undoubted case of mammary cancer has been recorded in a patient before the fifteenth year. There are very few examples recorded before the twenty-fifth year. The greatest number are met with in women, between the twenty-fifth and the fiftieth years. It may occur at any age after fifty, and has been observed in a woman, ninety years of age.

Although absolute ignorance prevails concerning the cause of cancer, few pathologists who have given special attention to the matter will admit that physical injury to a part can cause it to become cancerous.

The details of an actual case will serve to show how necessary it is to carefully follow up patients in order to avoid a false impression. In 1906 I removed the left breast of a married but childless woman on account of carcinoma; the axillary fat and lymph-glands were also removed. The patient made an uneventful recovery. The cancerous nature of the disease was established by a careful microscopical examination of the breast and the lymph-glands. In 1909 this woman again came under observation with a rounded lump in the right breast, which she attributed to a blow from a corner of a box which she received four months previously whilst struggling with another woman for the possession of the box. The lump in the breast was as big as a tennis ball, hard, and somewhat adherent to the skin. The nipple appeared to be normal. The condition of the tumour and its relation to the breast were quite unlike primary cancer, but resembled in many points secondary carcinoma of the breast, for I must point out to you that when the mammary gland is the seat of secondary cancer the disease assumes the massive form which is so often seen in metastatic cancer. In its clinical features the tumour resembled a mammary sarcoma, and the rapid growth following injury led me to entertain the idea

that this lump might prove to be sarcomatous. There was no doubt as to the advisability of removing the breast, and in the course of the operation it proved to be a cyst with unusually thick walls.

Sarcoma of the Breast. — It has already been mentioned that sarcomata are unusual tumours in the breast and that they constitute about 10 per cent. of the malignant tumours of this organ. Among recent statistics on this point may be mentioned those of Poulsen (Copenhagen): Among 335 tumours of the female breast 33 were sarcomata; and Gebele among 359 mammary tumours in Bergmann's klinik found 34 sarcomata. Schmidt found in 139 cases of malignant disease of the breast 126 examples of carcinoma and 13 of sarcomata. Horner among 172 malignant tumours of the breast found 14 sarcomata. Sarcoma occurs at an earlier age than cancer, and women are most liable to this form of malignant disease between the twentieth and fortieth years of life, whereas cancer is most frequent between the thirty-fifth and fiftieth years.

As with cancer, the patients often attribute the disease to an injury, especially to what may be called an "intensive injury." For example, a constable was kicked in the breast; about two months later he noticed a small lump at the seat of injury; this quickly increased and proved to be a sarcoma (Harrison Cripps).

A spinster, aged fifty years, employed as a cook, "let a round of beef fall on her breast"; it gave her a severe blow. A month later she noticed a small hard lump which gradually increased in size, and in two months it was as big as a penny. It then grew and formed a large tumour. The breast was freely removed, the disease quickly recurred, and the patient died within fifteen months of receiving the blow (Sir George Thomas Beatson).

A married woman, aged fifty-eight years, received a blow on the right breast; four months later she came under observation with a tumour in the breast which grew quickly; six weeks later it had grown to the size of a child's head. It was removed and proved to be a round-celled sarcoma. She returned four months later with a recurrence, and died within a year of receiving the injury (Schmidt).

Such clear and definite cases of injury being followed by a sarcoma as in the three preceding reports are certainly uncommon in the breast, but they are frequent in the limbs, especially in children and adolescents. There would be no difficulty in collecting a score of examples from current surgical literature. The following case came under the writer's notice: A man, aged twenty-one years, received a blow on the shin from a barrow loaded with bricks. One month later a swelling was noticed, and proved to be a round-celled sarcoma of the tibia as big as a cocoa-nut. Amputation was performed (Museum, Middlesex Hospital).

Every pathological museum of any pretensions contains specimens of sarcomata growing in bones of the head and the limbs as a sequel to a severe single physical injury. Such cases are by no means confined to the civilised inhabitants of the globe. A girl, aged sixteen years, a native of the Island of Mabuag, in Torres Straits, "fell down and hurt her knee, but did not break the skin." Shortly after this the knee began to swell, and in three months she came under the care of Dr. G. V. White, in Thursday Island, and the leg was amputated. The girl died two months after her return to Mabuag. Professor Allen, of Melbourne, examined the growth and found it to be a *periosteal* sarcoma ('Third Scientific Report of the Imperial Cancer Research Fund').

In the case of sarcomata we are met with similar facts to those surrounding the relation of trauma to

the incidence of cancers (carcinomata), namely, that surgeons see very many patients with sarcomata who cannot recall any preceding injury to the part; and of the enormous number of contusions and injuries only an infinitesimal proportion is followed by sarcomata. Small as is this number, the circumstances relating to these sequences are such as to lead surgeons to believe *that a single "intensive" injury may occasionally induce the growth of a sarcomatous tumour*, and to place it outside the category of mere coincidence.

The attitude of surgeons as reflected in their writings concerning the influence of trauma, or physical insults, as an ætiological factor in the production of malignant tumours in the breast, justifies the following statement:

In regard to cancer (carcinoma) all surgeons of experience admit that there is a definite history of intensive mechanical injury in about 10 per cent. of the patients. They are very careful not to express a definite opinion as to the causal relationship of such injuries to the formation of cancer in the breast. There is also a paucity of published statements from surgeons of great experience affirming trauma as a cause of mammary cancer.

In regard to sarcoma of the breast, there is a definite opinion held by experienced surgeons to the effect that there are many carefully observed and thoroughly reported cases in which primary sarcoma of the breast has quickly supervened on a single intensive injury. The sarcomatous nature of such tumours has been ascertained by a microscopic examination at the hands of a competent pathologist, and their malignant nature has been confirmed by the early death of the individual. It is undeniable that a single intensive blow or knock on the breast may be occasionally followed by a sarcomatous tumour.

There is, however, a wide diversity of opinion as to

the exact conditions under which any given case of tumour is to be regarded as of traumatic origin. All agree that the situation of the tumour must correspond to the site of the injury, but there is no definite agreement among surgeons as to how long an interval may elapse between the injury and the appearance of the tumour in order that they may be regarded as cause and effect. This can only be decided by a careful study of individual cases.

In relation to this subject it is necessary to mention that of all the tumours, benign or malign, which attack man, sarcomata are the most difficult, from the clinical and histological points of view, to distinguish from a simple inflammatory or from an infective swelling.

It is undesirable to conclude this lecture on trauma in relation to cancer and sarcoma without referring to a class of tumour directly depending on injury. I refer to those interesting cysts met with chiefly on the fingers, the cornea, and iris, due to the accidental embedding or implanting of minute portions of cutaneous epithelium. These "implantation cysts," as I ventured to name them some years ago, appear chiefly on the volar surface of the fingers, and vary in size from a split-pea to a cherry (Fig. 28). These cysts lie in the loose tissue of the skin, and if the skin which covers them is carefully examined you will, as a rule, find a scar. Careful accounts of these cysts were published many years ago by Le Fort (1881) and Polaillon (1884). These surgeons recognised that such cysts were due to small fragments of skin, sometimes containing hair-follicles and sweat-glands, which have been carried into the subcutaneous tissue by a penetrating foreign body. This implanted skin becomes encapsuled by connective tissue and develops into a cyst.

Accidents which lead to the formation of such cysts occur in a variety of ways, such as punctures by awls, forks, needles, thorns, glass, knives, bites, lacerations,

and incisions made in the course of surgical operations, and by shot.

When such a cyst is examined microscopically, especially one from the pulp of the finger, "it appears as if a piece of skin had been inverted." In others the implanted epidermis appears to be shed in layers, and thus produces a laminated appearance; in one instance the cyst contained a fragment of a bullet. Wieman has twice found foreign bodies in implantation cysts.

The belief that these cysts arise from fragments of the epidermis accidentally implanted into the subcutaneous tissue is confirmed by what we know of similar cysts on the iris and cornea associated with mechanical injury. Hulke (1869) studied the microscopic features

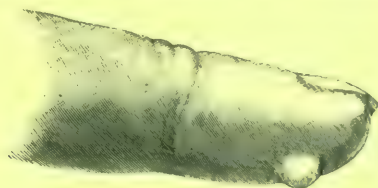


FIG. 28.—An implantation cyst in the skin of the finger.

of certain small cysts occasionally found on the iris, and found that some of them contained sebaceous material, such as fills the cavities of dermoids; he stated that in a large proportion of cases there was a distinct history of antecedent mechanical history, and he suggested that some of these cysts originated from portions of Descemet's membrane torn from the cornea and implanted on the iris. Many instances are now known in which eyelashes have been implanted on the iris by foreign bodies, such as knives, forks, needles, foils and the like penetrating the cornea. Even so gross a weapon as a sword has brought about such an event, as in the case of Barry Sullivan. This actor was playing in Shakespeare's famous tragedy, "Richard III," and in Act v, Scene iv, in which is represented the combat

between Richard and Richmond, some spirited sword-fighting occurs. In this encounter Barry Sullivan received an accidental perforating wound in the eye. Later a cyst containing an eyelash grew from his iris (see Treacher Collins, 'The Anatomy and Pathology of the Eye,' 1896).

Similar implantation cysts occur in the cornea after gunshot injuries, blows from tip-cats, and in the lines of incisions made for the extraction of cataracts, etc.

I have drawn your attention to this matter as a prelude to some interesting pathological processes which occasionally occur in the abdomen as sequelæ to mechanical injuries of ovarian cysts. When a woman has a large ovarian cyst one of the dangers she runs is rupture of the cyst from violence: for example, a cyst of this kind has been burst during an "immoderate fit of laughter"; in stooping to button the boots; during manipulation by a physician; during vomiting or coughing. A common cause is a fall, either from a chair, a carriage, or in alighting from a gig. When the cyst contains clear fluid it is quickly absorbed and excreted as urine. In the case of a purulent cyst it would probably have a fatal termination. When the tumour is a dermoid (embryoma), the grease, hair, and epithelial cells it contains are scattered over the abdominal viscera, the cells become engrafted on the peritoneum, and in some instances hundreds of minute dots, each furnished with a tuft of hair, have been found. Occasionally these bodies are pedunculated and form cysts as big as bantam eggs. In the majority of such cases there was distinct history of mechanical injury. The relation of these nodules to the peritoneum is different to what is found where secondary nodules of cancer grow in relation with this serous membrane. The cells from dermoids engraft themselves on, but do not penetrate, the peritoneum, but in the case of the cancer-cells this membrane is

eroded and penetrated by them, the cells exhibiting the same invasive property so characteristic of them in other situations. It has long been known that when aseptic foreign bodies are introduced, or find their way into the general peritoneal cavity, they become quickly coated with an exudate (for convenience we call it "lymph"), which quickly organises and forms a fibrous capsule. This capsule is known as a cyst. Collections of fluid, such as blood and serum, are often encysted in this way. An interesting condition is often found when a papillomatous cyst of the paroöphoron bursts and scatters its cell-containing fluid far and wide in the belly. These cells become engrafted and grow into warts, and in some cases I have found warts or papillomata produced under these conditions contained in definite, complete, and independent cysts. Nowhere in the body can cyst-production of this kind be studied so completely as in the belly, but it assists us in appreciating the fact that the iris, the cornea, and the subcutaneous tissue generally possess the power of throwing a capsule around intruding epithelium.

I have dealt with these matters in connection with trauma in relation to tumours because, in the present condition of the law, cases are bound to arise in which your opinions will be sought in regard to the effects of injuries on pre-existing cysts and tumours, as well as on the debatable question of trauma as an ætiological factor in causing malignant disease. In such matters the old adage applies, "To be forewarned is to be forearmed," and, as some of you will quickly learn, lawyers are often cunning men.

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Bland-Sutton, (Sir) John
Cancer clinically considered.

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